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3rd Croatian Congress on Alzheimer's Disease with international participation

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Croatian Society for Neuroscience

UNDER THE AUSPICES OF

Alzheimer's Disease International

City of Zagreb

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CONGRESS TOPICS

1. NEW ASPECTS IN BASIC RESEARCH OF ALZHEIMER'S DISEASE
2. CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE
3. CURRENT TRENDS IN ORGANIZATION OF SELF-HELP GROUPS AND CARE-GIVERS EDUCATION

NEXT CONGRESS

4th Croatian Congres on Alzheimer's Disease
September 25th-28th, 2008, Brijuni, Croatia

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The Editor-in-Chief of "Neurologia Croatica" with the advice of Editorial Board, accepted the publishing of the abstracts of the 3rd Croatian Congress on Alzheimer's Didease with international participation as a supplement of the journal.

The editors of this supplement have been committed to review and accept the abstracts of the submitted contributions. The authors of the invited lectures are responsible for their own contributions.

The Supplement Coordinating Editor is responsible of the overall quality of the supplement.

N. Zurak
Editor-in-Chief

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POSTER PRESENTATIONS

INTRODUCTION

The Alzheimer Disease Societies Croatia (ADSC), with support of the Croatian Society for Clinical Psychiatry, CMA and the Croatian Society for Neuroscience has undertook organization of the 3rd Croatian Congress on Alzheimer's Disease with international participation, a scientific gathering aimed at highlighting the problem of an increasing number of people affected by Alzheimer's dementia (AD) in modern societies.

This being the year when the 100th anniversary the disease recognition is marked worldwide, we have decided to join the celebrations and set up a sculpture exhibition "In Honour of Alois Alzheimer" by our colleague Dr Eduard Pavlović.

To get a broader picture of AD, which will certainly become a priority medical problem of the 21st century, it was decided that the Congress should focus on three aspects: basic sciences, clinical sciences and self-support groups. Each of these topics will be presented by distinguished invited speakers. We are honoured that the Congress will open with a lecture by Christine McGregor, representative of Alzheimer's Disease International (ADI), the umbrella organization the ADSC recently joined as a provisional member. It is also a great honour for the organizer that Dr Jack Diamond, Scientific Director of Alzheimer Society of Canada will render an educational lay-lecture about AD. We shall have to chance to learn about the most recent results of the European and Croatian neuroscientific laboratories, and the esteemed international and national clicians will inform us about new pharmacological treatments and care for people with dementia. The Congress program has been conceived so that it offers a comprehensive approach to AD on a daily basis and gives a chance to experts and all interested persons coming from various professions to exchange information and experiences. We have left a considerable opening for questions and discussions from which the participants should benefit the most. Since we did not envisage organisation of parallel sections, a large number of submitted papers will be presented in poster form, and the posters shall remain exhibited for the Congress duration and be discussed at coffee breaks.

We would like this Congress, organized biannually here on the Brijuni Islands, to become a traditional and unique focal point in Croatia fostering a comprehensive and holistic approach to AD, and summoning all relevant Croatian and numerous international experts and stakeholders involved in AD and related fields.

Primarius Ninoslav Mimica, M.D., D.Sc.

Scientific Director & Vice-President of Alzheimer Disease Societies Croatia

President of the Organizing Committee of 3rd Croatian Congress on Alzheimer's Disease

WELCOME

Dear colleagues and friends,

it is my great pleasure and honour to address this third Croatian congress on Alzheimer's disease. I am delighted to see so many distinguished scientists and clinicians from across the world participating in this meeting to share their views and experience.

At this point, I would like to remind you that, since the first description of Alzheimer's disease 100 years ago, basic and clinical research on this disorder went through many hurdles. The three probably most unfortunate assumptions that turned investigations into the "blind alley" were first, the naming of the disease as "dementia praecox" (Kraepelin, 1910) due to the fact that the first 15 patients described were younger than 65. This erroneous concept lasted for almost sixty years until, in 1968, a large epidemiological study carried by Blessed, Tomlinson and Roth showed that Alzheimer's disease can begin at any age in adults (Br J Psychiat 114:797). The second false, yet commonly held misperception, was the belief that the disease cannot be caused by single gene mutations. After a long-lasting search, this was finally disproved in 1991, when Hardy and colleagues described the first mutation of the gene for amyloid precursor protein on chromosome 21 (Nature 349:704). Finally, the last and most recent negative blow was failure of immunization using the whole amyloid beta molecule (vaccine AN1792) which caused inflamatory response and meningoencephalitis (vaccination was stopped on 21st March 2002).

As to the current state of affairs in the field it can be said that it looks promising due to the fact that two complementary modalities, biomarkers in cerebrospinal fluid and magnetic resonance imaging have been improved to a level that very early diagnosis of Alzheimer's disease became possible (Hansson et al., Lancet Neurol 2006;5:228). In the near future, we can expect even more precise determination of the primary cause of dementia using molecular analysis of cerebrospinal fluid and imaging of brain structure and activity. It can also be expected that, besides the currently registered drugs for early (donepezil hydrochloride, galantamin hydrobromide, tacrine hydrochloride) and moderate/late Alzheimer's disease (memantin), new drugs, such as gamma-secretase inhibitors, will be developed to act more effectively on the key pathophysiological events of the disease.

The program of the forthcoming third meeting focuses on many of these exciting new advances on Alzheimer's disease, including functional molecular profiling, diversity of the tau gene, cerebrospinal fluid and other peripheral biomarkers, monoclonal antibodies as research and diagnostic tools, brain insulin receptor signaling, neuroimaging methods and the role of cholesterol and gangliosides/glycosphingolipids metabolism. How close we are to the solution of therapy of Alzheimer's disease will be discussed in several sessions. We will hear about the newest research findings in many closely related fields, covering topics from other dementing conditions such as Lewy body disease and tauopathies to the production and use of neural stem cells and telomere dynamics during aging.

On behalf of the Scientific Committee of the 3rd Croatian Congress on Alzheimer's Disease I warmly welcome all of you to Brijuni to enjoy this stimulating meeting, which will also provide you an opportunity to experience the Croatian late summer on the beautiful Adriatic coast. I thank you all for your contribution.

With compliments,

Goran Šimić

ORAL PRESENTATIONS

NEW ASPECTS IN BASIC RESEARCH OF ALZHEIMER'S DISEASE

OP-B-(01-12)

3rd Croatian Congress on Alzheimer's Disease with international participation
Neurol. Croat. Vol. 55 (Suplement 4) 1-108 (2006)

COMMON DIVERSITY OF THE TAU GENE IN AZHEIMER'S DISEASE AND NEURODEGENERATION

DE SILVA R[1], Pittman A[1], Myers, A[2], Hardy J[2], Lees A[1]

[1] *Reta Lila Weston Institute of Neurological Studies, University College London, London, UK*
[2] *NIA/NIH, Bethesda, MD, USA*
rsilva@ion.ucl.ac.uk

Aims: Several mutations in the microtubule associated protein, tau *(MAPT)* gene cause frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17). Defective tau protein is also implicated in sporadic tauopathies including Alzheimers disease (AD), progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD), due to the hallmark insoluble deposits of fibrillar tau in the neuronal and glial inclusions. Although *MAPT* is not mutated in these tauopathies, association of a common genetic variation of *MAPT* with PSP and CBD has long been established. The aim of our work was to identify the functional basis of this increased risk by fine-mapping the tau gene and investigating potential functional polymorphisms by cell-based assays and real-time PCR.

Methods: From HapMap data, we derived 6 haplotype-tagging SNPs (htSNPs) which account for over 90% of the haplotypic diversity of *MAPT*. Using these htSNPs, we identified a single H2 haplotype and multiple haplotypes representing the H1 clade and carried out association studies in several case-control series of pathologically confirmed PSP, CBD and AD.

Results: The MAPT H1 and H2 haplotypes evolved separately, without any evidence of H1/H2 recombination. The H1 clade consists of multiple sub-haplotypes of which H1c is highly associated with PSP ($p<0.001$), and, to a lesser extent, AD ($p=0.004$) and CBD ($p=0.066$). The other common sub-haplotype, H1b, is not associated. The sole H2 haplotype has a strong negative association with PSP ($p=0.0003$) suggesting a protective mechanism. Using a cell-based luciferase reporter assay and real-time PCR quantitation of tau gene expression in flash-frozen brains, we showed that overall *MAPT* and four-repeat tau mRNA expression is significantly higher off the H1c allele, compared to H1b and significantly lower in H2 *MAPT*.

Conclusion: Increased expression of genes involved in disease pathogenesis in PD (SNCA) and AD (APP) due to gene multiplications, causes disease in some familial cases. We for the first time show that the basis of the association of common variation of *MAPT* with sporadic PSP, CBD and AD could be due to increased expression of the *MAPT* H1c risk allele. We are currently investigating the critical sequence elements and trans-factors that differentially modulate *MAPT* expression and splicing.

NEW ASPECTS IN BASIC RESEARCH OF ALZHEIMER'S DISEASE (OP-B-02)

MORPHOLOGICAL CHARACTERIZATION OF HUMAN NEUROSPHERES

DIANA A

Department of Cytomorphology, Monserrato (Cagliari), Italy
diana@unica.it

Neural stem cells (NSCs) represent the most primordial and least committed cells of the nervous system, with self-renewal and multipotentiality features that exist before regional specification develops. In the in vitro setting, stem cells grow in suspension as spherical aggregates (neurospheres) when supplemented with EGF and/or FGF-2. Neurospheres contain multipotent stem cells normally present in very low number and "progenitors" or "precursors" that are more restricted in their proliferative potentials and lineage commitment within the neuropoietic pathway. In the last decade, intensive investigation has been carried out in order to identify and tracking neural stem cells during the process of differentiation into functional and mature cells by means of rigorous selection markers. Nevertheless, a systematic morphological characterization of neurosphere forming cells is still lacking. In order to fill such a gap of knowledge, we studied human neurospheres derived from whole brains of 8-12 week-old embryos within a proliferating period up to 1 year by the use of conventional fluorescence microscopy, confocal microscopy, transmission (TEM) and scanning (SEM) electron microscopy. The work presented in the talk will address the following points: the difficulties of drawing unambiguous nomenclature to distinguish cellular subpopulations based on the expression of overlapping immunocytochemical markers (i.e. nestin and GFAP) ; the meaningful contribution of three-dimensional reconstruction of optical neurosphere sections for a broader elucidation of structural arrangements; the complexity of cytoarchitecture revealed by ultrastructural analysis as a result of coexisting events of mitogenic, apoptotic and phagocitic interactions; the intriguing heterogeneous appearance of cells covering the outer layers of neurospheres intermingled with ramified processes and or fiber-like structures by SEM observation.

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ALZHEIMER'S DISEASE, MODIFICATIONAL TREATMENT - PERSPECTIVES

IVKIĆ G[1], Erdeljić V[2], Radonić E[1]

[1] *Croatian Institute for Brain Research, School of Medicine, Zagreb, Croatia*
[2] *University Hospital Center Zagreb, Zagreb, Croatia*
givkic@hiim.hr

Despite the intense research on ethiology and pathogenesis of scientific neurodegenerative diseases, the pathogenesis of Alzheimer's disease and related neurodegenerative diseases, are still remaining unknown.

With respect to therapy, the major problem is leak of causal treatment. Currently available drugs have exclusively symptomatic effects and do not significantly modify the course of disease. In general, there are three possible approaches to modifying the course of the disease:

1. acting on specific aspects of AD pathology,
2. generally neuroprotective or neurotrophic effects,
3. approaches based on epidemiological observations.

This presentation is aimed to illustrate all three of the above mentioned options. Especially we want to stress the strategies that directly act on amyloid generation, which is currently the most active field of investigation. Approaches presented in this work emphasize:

- secretase inhibition,
- inhibition of amyloid- aggregation,
- immunotherapy and,
- strategies with possible indirect effect on amyloid generation.

NEW ASPECTS IN BASIC RESEARCH OF ALZHEIMER'S DISEASE (OP-B-04)

COMPOSITION AND METABOLISM OF GANGLIOSIDES IS ALTERED IN NEURAL AND NON-NEURAL TISSUE IN ALZHEIMER'S DISEASE

KALANJ BOGNAR S[1], Heffer Lauc M[2], Vukelić Ž[3], Rundek T[4], Talan Hranilović J[5], Demarin V[6]

[1] *Croatian Institute for Brain Research, School of Medicine, Zagreb, Croatia*
[2] *Department of Biology, School of Medicine Osijek, Osijek, Croatia*
[3] *Department of Chemistry and Biochemistry, School of Medicine Zagreb, Zagreb, Croatia*
[4] *Department of Neurology, Columbia University College of Physicians and Surgeons, New York, NY, USA*
[5] *Ljudevit Jurak Department of Clinical Pathology, Zagreb, Croatia*
[6] *Department for Neurology, Sestre Milosrdnice University Hospital, Zagreb, Croatia*
svjetla@mef.hr

Background: The biological roles of gangliosides/glycosphingolipids (GSL) have been extensively studied and their involvement in key cellular events as well as their particularly important functions in animal brain tissue are well known. The idea that there are alterations in glycosphingolipid metabolism in Alzheimer's disease (AD) arose from biochemical studies of brain gangliosides pattern. Changes in content and composition of gangliosides and other membrane lipids in AD brain regions were documented by several groups, including ours. Observed specific alterations of ganglioside pattern in AD brains were mostly discussed as a consequence of: (a) neuronal cell degeneration, demyelination and gliosis; (b) accelerated lysosomal degradation of gangliosides. Increased expression of lysosomal hydrolases in neuronal populations affected by amyloid pathology was indeed documented by other groups. This finding was explained as a proof for up-regulation of endosomal-lysosomal system in AD and was proposed to be an early marker of metabolic dysfunction related to primary AD etiopathogenesis.

Methods and Results: A speculation that alteration of ganglioside metabolism/catabolism occurs also in nonneural tissue in AD was further studied by our group. In our study the activity of several enzymes involved in ganglioside and sulfatide catabolism (ß-galactosidase, ß-hexosaminidase, -hexosaminidase A and arylsulfatase A) was analyzed in leukocytes and skin fibroblasts derived from individuals with AD and Down's syndrome (DS). Our results showed statistically significant increase in ß-galactosidase activity in AD and DS leukocytes in comparison with age-matched control leukocytes. Also, increased activity of ß-galactosidase and ß-hexosaminidase was observed in AD and fetal DS skin fibroblast cell line and age-matched controls obtained

from commercial sources as well as in several DS and age-matched control skin fibroblast cultures established in our laboratory.

Conclusions: Obtained results indicated that acceleration of at least some lysosomal catabolic pathways of gangliosides is present in AD and DS nonneural cells (leukocytes and skin fibroblasts). These findings raised several interesting questions: first, whether detected changes of glycosphingolipid metabolism in peripheral cells may present as peripheral biochemical markers in AD; second, is there a change in transcriptional regulation of analyzed enzymes in AD; third, are there mutations in genes coding for GSL biosynthetic/catabolic enzymes which may contribute to complex AD pathogenesis; fourth, which other (epigenetic) events modify and cause altered enzyme activities in both AD and DS.

NEW ASPECTS IN BASIC RESEARCH OF ALZHEIMER'S DISEASE (OP-B-05)

MONOCLONAL ANTIBODIES AS RESEARCH AND DIAGNOSTIC TOOLS IN NEUROMUSCULAR AND NEURODEGENERATIVE DISEASE.

MORRIS G

Centre for Inherited Neuromuscular Disease (CIND), RJAH Orthopaedic Hospital, Oswestry, UK
glenn.morris@rjah.nhs.uk

Monoclonal antibodies (mAbs) against proteins are well-known for their high specificity, as well as their availability in almost limitless supply, making them powerful reagents for immunolocalization of antigens in cells and tissues. This specificity can often be enhanced by identification of their precise binding sites on the antigen by procedures known as "epitope mapping".

Methods for monoclonal antibody production will be reviewed with particular emphasis on screening methods to obtain the desired specificities. Methods for epitope mapping include chemical and enzymatic digestion, mass spectrometry and phage-displayed peptide libraries, as well as genetic manipulation methods for recombinant antigens.

Antibody binding is invariably dependent on the protein structure of the antigen and this can cause problems for research applications of antibodies. Immunolocalization with antibodies may be dependent of the method of fixation and antibodies that work well in western blotting may not be useful for immunolocalization at all. Masking of epitopes by other proteins or macromolecules in cells or tissues can also affect the validity of immunolocalization studies.

In relation to neurodegenerative disease, we have produced panels of mAbs against huntingtin and dopamine receptors to study the distribution of these proteins in the brain. Specific degeneration of lower motor neurons is responsible for spinal muscular atrophies and we will show how mAbs generated against the proteins affected by this genetic disorder are throwing light on the degenerative mechanism. In genetic muscular dystrophies, such as Duchenne and Emery-Dreifuss, a unified hypothesis is emerging to explain how mutations in both plasma membrane and nuclear membrane proteins may cause related clinical features. In myotonic dystrophy, we are just beginning to understand how a trinucleotide repeat expansion can cause such a wide range of clinical features in muscle, brain and many other tissues.

Research at CIND is supported by the Muscular Dystophy Campaign (UK), the Muscular Dystrophy Association (USA), Families of SMA (USA), National Institutes of Health (USA), Association contre les Myopathies (France) and the Henry Smith Charity (UK).

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PERIPHERAL BIOCHEMICAL MARKERS IN ALZHEIMER'S DISEASE

MÜCK-ŠELER D[1], Mimica N[2,3], Pivac N[1], Mustapić M[1], Deželjin M[1], Pavlović M[4], Folnegović-Šmalc V[2,3]

[1] *Ruđer Bošković Institute, Zagreb, Croatia*
[2] *Psychiatric Hospital Vrapče, Zagreb, Croatia*
[3] *School of Medicine, University of Zagreb, Zagreb, Croatia*
[4] *Institute for Medical Research and Occupational Health, Zagreb, Croatia*
seler@irb.hr

Aim: Alzheimer's disease (AD) is a multifactorial and complex disorder. The age of the onset and the course of AD could be related to the lifestyle, genetic, socidemographic, environmental, clinical and pharmacological factors. Post mortem brain studies indicated that the alterations in neurotransmitters systems could be involved in the ethiology of AD. The aim of the study was to determine peripheral biochemical markers (platelet serotonin/5-HT/ concentration, platelet monoamine oxidase type B /MAO/ and plasma dopamine-beta hydroxylase /DBH/ activity) in patients with AD subdivided according to the onset of disease and to the presence of psychotic features.

Methods: The diagnosis of the probable AD fulfilling NINCDS-ADRDA criteria was established according to the ICD-10 and DSM-IV-TR criteria. Mini Mental Status Examination (MMSE) was used to assess the cognitive impairment. The study included 43 male and 144 female patients with AD subdivided in two groups according to early (before the age of 64 years) or late (after the age of 65 years) onset of AD. The control group consisted of sex and age-matched drug free healthy subjects (65 female and 51 male) with no history of the psychiatric illness. Platelet 5-HT concentration and platelet MAO activity were determined using spectrofluorimetric methods, and plasma DBH using photometric method.

Results: The platelet MAO activity was higher in female patients with early and late and male patients with early onset of AD as compared to healthy controls. The pronounced increased in platelet MAO activity was observed in AD patients with nonpsychotic features. Plasma DBH activity was significantly lower in patients with AD. There were no significant difference in platelet 5-HT concentrations among groups. Conclusions. The ethiology and progress of AD could be connected with the changes in the biochemical parameters. The results of this ongoing study, support the presumption that platelet MAO and plasma DBH activity could be used as a biological marker for different categories of AD. Our results of the altered MAO and DBH activity in patients with AD, support the presumption that toxic and reactive metabolites of catecholamine neurotransmitters could be involved in the ethiology of AD.

NEW ASPECTS IN BASIC RESEARCH OF ALZHEIMER'S DISEASE (OP-B-07)

PREDICTIVE GENETIC TESTING OF ALZHEIMER'S DISEASE - A PUBLIC PERSPECTIVE

ORUČ L[1], Kapur L[2], Pojskić N[2]

[1] *Psychiatric Clinic, Clinical Center, University of Sarajevo, Bosnia and Herzegovina*
[2] *Laboratory for Human Genetics, Institute for Genetic Engineering and Biotechnology, Sarajevo, Bosnia and Herzegovina*
loruc@bosna.ba

Alzheimer disease (AD) is the most common cause of adult-onset progressive degenerative dementia and clearly complex in its etiology. Genetic factors are known to have a key contribution to development of AD. Although several vulnerability genes are identified and well characterized, some familial cases of this disease are due to rare mutation in other genes. Majority of AD cases are late-onset. Although APOE epsilon 4 allele function as a crucial risk factor for it, the risk of AD appears to be heterogeneous in its nature with additional genetic risk factors interplay. Several certified genetic test for prediction of AD are commercially available. Its certainty is complicated by inability to assess all possible potent risk factors. Additionally, genetically based prediction of AD onset is questioned due to general ethical and social issues, concerning benefits but also potential harm.

However little is known about public standpoints towards predictive genetic testing in neuropsychiatric disorders as AD. This presentation argues main issues related to predictive genetic testing for complex disorders supplemented with data from Bosnia and Herzegovina.

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GENETIC ANALYSIS OF CATECHOL-O-METHYL-TRANSFERASE IN ALZHEIMER'S DISEASE

PIVAC N[1], Deželjin M[1], Mustapić M[1], Mimica N[2,3], Folnegović-Šmalc V[2,3], Mück-Šeler D[1]

[1] *Ruđer Bošković Institute, Zagreb, Croatia,*
[2] *Psychiatric Hospital Vrapče, University Department of Psychiatry, Zagreb, Croatia*
[2] *School of Medicine, University of Zagreb, Zagreb, Croatia*
npivac@irb.hr

Aim: Alzheimer's disease (AD) is a growing public health problem, the major risk for dementia, frequently associated with psychotic symptoms. The causes of AD are still unknown, and it is assumed that various etiologies lead to the characteristic pathological changes. Around 5-10% of AD is influenced by genetic factors. The aim of the study was to determine the genetic variations in catechol-O-methyltransferase (COMT), the major dopamine (DA) degrading enzyme, in patients with AD. The most common polymorphism of COMT is a single base change which constitutes of guanine to adenine substitution at the exson 4 of the COMT gene. This is a functional polymorphism responsible for substantial variability in COMT enzymatic activity. At position 158, a valine is replaced by methionine. The valine allele is associated with high COMT activity, and up regulation of striatal DA activity, carrying an increased risk for schizophrenia and a susceptibility to psychosis in AD, whereas the methionine allele is associated with low COMT activity, and a higher propensity for violence and suicide.

Methods: The diagnosis of the probable AD fulfilling NINCDS-ADRDA criteria was established according to the ICD-10 and DSM-IV-TR criteria. Mini Mental Status Examination was used to assess the cognitive impairment. The study included 62 AD patients: 30 with late onset (AD started after 65 years of age) and 32 with early onset (AD started before 65 years of age), and 90 drug free healthy subjects. Genotyping methods: DNA isolated from blood by a standard salting out procedure was genotyped for the COMT G/A polymorphism with ABI Prism 7000 Sequencing Detection System apparatus (ABI, Foster City, USA) using Taqman-based allele-specific polymerase chain reaction assay (TaqMan Drug Metabolism assay), according to the procedure described by the Applied Biosystems, and using the primers and probes from Applied Biosystems (ABI, Foster City, USA).

Results: The homozygous GG (valine) genotype was found in 28%, homozygous AA (methionine) genotype in 20%, while heterozygous GA genotype was determined in 51% subjects, with no significant deviation from the Hardy - Weinberg distribution ($p>0.50$). The distribution of GG, AA and GA genotypes was 27, 27 and 47% for patients with late onset of AD; 25, 22 and 53% for patients with early onset of AD; and 30, 18 and 52% for control sub-

jects, respectively. The frequency of the COMT genotype (2 =0.012; df=1; p=0.913) was similarly distributed among patients with early and late onset of AD, or between patients with AD and control subjects (2 =1.004; df=1; p=0.605).

Conclusion: These preliminary data do not support the hypothesis that valine variant encoded by the G allele is associated with the occurrence of AD. COMT polymorphism modulates cognitive functions and high activity carriers, due to the different regulation between striatal and frontal DA activity, are prone to develop psychotic symptoms. Therefore, our further study will correlate COMT polymorphism with psychotic symptoms (delusions, hallucinations and nighttime disturbances) in AD.

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TELOMERE DYNAMICS IN CELL AND ORGANISMAL AGING

RUBELJ I

Ruđer Bošković Institute, Zagreb, Croatia
rubelj@irb.hr

Aim: A strong stochastic component has been described for the appearance of senescent cells in proliferating cultures. For example, two cells arising from a single mitotic event can exhibit large differences in their doubling capacities. In our previous work, we presented a molecular model that explains the observed stochastic phenomena. The model is based on a combination of both, gradual telomere shortening (GTS) and abrupt telomere shortening (ATS), so that GTS occurs as a consequence of exonuclease degradation of the 5' strand at telomere ends and ATS is predicted to occur through strand invasion of the 3' overhang into the telomeric/subtelomeric border region followed by formation of a t-loop structure. ATS is mediated by Holiday structure formation which results in a deletion of distal telomeric repeats through circularisation. Our model explains the gradual increase of senescent cells in a culture by proposing that long telomeres have a stable conformation and a low probability of undergoing abrupt shortening but, as telomere shortening progresses the probability of conformation changes to an unstable form increases almost exponentially. Abrupt shortening of one or more telomeres in the cell causes cell cycle arrest within one cell division. Since it was published, many features of our model have been demonstrated both structurally and functionally including the presence of ultrashort, single telomeres in senescent human cells, the identification of circular telomeric DNA in various mammalian cell lines, generation of t-loop-sized deletions at human telomeres by homologous recombination in ALT cells etc. Methods: In order to further analyze this phenomenon senescent cells were separated from young cycling cells by BrdU incorporation followed by Hoechst dye/light treatment.

Results: We did not observe difference in telomere lengths between these two fractions of cells, which is expected according to ATS model.

Conclusion: Our results demonstrate that telomeres of early-senescing cells are the same length, and must shorten at the same rate, as cycling sister cells in the culture, which is the expected result if abrupt shortening of a single telomere triggers the onset of cell senescence rather than accelerated shortening of all telomeres in a subpopulation of cells.

NEW ASPECTS IN BASIC RESEARCH OF ALZHEIMER'S DISEASE (OP-B-10)

BRAIN INSULIN RECEPTOR SIGNALING CASCADE IN EXPERIMENTAL RAT MODEL RELATED TO THE HUMAN SPORADIC ALZHEIMER'S DISEASE

ŠALKOVIĆ-PETRIŠIĆ M[1], Grünblatt E[2], Hoyer S[3], Riederer P[2]

[1] *Department of Pharmacology and Croatian Institute for Brain Research, School of Medicine, University of Zagreb, Zagreb, Croatia*
[2] *Department of Clinical Neurochemistry, University Department of Psychiatry and Psychotherapy, University of Würzburg, Würzburg, Germany*
[3] *Department of Pathology, University Clinic, University of Heidelberg, Heidelberg, Germany*
melitas@mef.hr

Aim. Due to the slow, often imperceptible onset, and nature of the sporadic Alzheimer's disease (sAD), initial pathophysiological changes and their further course in the human brain are unknown, making the search for an appropriate experimental model even more difficult. Decreased brain glucose/energy metabolism and cognitive deficits similar to those found in sAD, were reported in streptozotocin (STZ)-intracerebroventricularly (icv) treated rats, suggesting them as a probable experimental model of this disease. Study was aimed to explore the elements of brain insulin receptor (IR) signaling cascade and time-course of their changes in STZ-icv treated rats.

Methods. Cognitive deficits (Morris Water Maze Swimming Test), neurochemical changes of IR signalling cascade elements (Western blot), gene expression changes of insulin-like growth factor 1 (IGF-1) receptor (quantitative-RT-PCR) and structural changes in beta amyloid aggregates (Congo red staining) in the brain of STZ-icv (1 mg/kg) rats, were measured ≤three months following the STZ-icv treatment.

Results. Hippocampal protein kinase B/Akt levels were mildly but insignificantly increased after one month, and mildly but significantly decreased (-9%) three months after STZ treatment. In line with that, the relative phosphorylated/non-phosphorylated glycogen synthase kinase-3α/β, pGSK-3α/β /GSK-3α/β ratio in hippocampus was found significantly increased (+50%) after one, and decreased (-9%) after three months. Mild increase in hippocampal total tau expression was found one month after STZ-icv treatment. Diffuse congophilic, beta amyloid-like aggregates were found in the meningeal capillaries three months after STZ-icv treatment. mRNA expression of IGF-1 receptor which shares signaling cascade pathway with IR and could compensate IR dysfunction, has been found decreased in the brain of STZ-icv treated rats. Neurochemical and structural changes in STZ-icv treated rats were accompanied by cognitive deficits that were more pronounced with a longer duration of post-treatment period (-46% after three months vs. -33% after one month)

Conclusion. STZ-icv rat model shares similarities with human sAD at the behavioural, structural and neurochemical level, and suggests that brain IR signaling alterations, observed in humans post-mortem mostly in the late stage of disease, may in fact be an early trigger in sAD generation.

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NEW ASPECTS IN BASIC RESEARCH OF ALZHEIMER'S DISEASE (OP-B-11)

PATHOLOGICAL SUBSTRATES OF ALZHEIMER'S DISEASE: REVIEW AND NEED TO UPDATE CRITERIA WITH CSF BIOMARKERS

ŠIMIĆ G

Croatian Institute for Brain Research, Department of Neuroscience, Zagreb, Croatia
gsimic@hiim.hr

The first **NIA** (National Institute on Aging) neuropathological diagnostic criteria for AD, were based on quantification of minimal SP (senile plaques) cortical densities as a function of age *(Khachaturian Z.S., Arch. Neurol. 1985).* They were not broadly accepted because SP formation may be partly a benign age-related phenomenon (making criteria less sensitive), the cortical region for quantification as well as the role of the clinical history were not well defined (making criteria less specific and non-comparable) and NFT (neurofibrillary tangles) were not considered. Therefore, another set of standardized criteria known as **CERAD** (Consortium to Establish a Registry for Alzheimer's disease) was proposed *(Mirra S.S. et al., Neurology 1991).* These semiquantitative criteria were determined as a function of the development of neocortical NP (neuritic plaques) in the superior temporal gyrus, prefrontal cortex and lower parietal lobule using modified Bielschowsky or thioflavin S staining in three age groups (less than 50, 50 to 75, and over 75 years). Based on the combination of clinical information and NP score, three levels of diagnostic certainty were assessed (definite, probable, or possible AD). Besides the fact that the hippocampal formation was again absent from criteria (despite its characteristic and crucial involvement in the initial stages of typical AD), the major weakness of CERAD criteria was that they relied only upon the amyloid cascade hypothesis and did not consider neocortical NFT, although these are not present in normal aging (except in entorhinal cortex) and correlate strongly with dementia severity *(Bierer L. et al., Arch. Neurol. 1995).*

In an attempt to reconciliate the amyloid cascade hypothesis with the major role of NFT in clinicopathological correlations, in 1997, the more rigorous **NIA-RI** (Reagan Institute) consensus recommendations for the postmortem diagnosis of AD were issued. These procedures use CERAD protocols for tissue processing, as well as semiquantitative assessment of AD lesions that must be made in several neocortical areas, hippocampus, substantia nigra and locus coeruleus and they also take into account the Braak staging system. In contrast to CERAD criteria which incorporate clinical data to provide a neuropathological diagnosis, NIA-RI criteria primarily aim to define the likelihood that clinical dementia was really due to AD lesions. Because NIA-RI criteria take into account the number of neocortical NFT, in comparison to CERAD

they are more specific but less sensitive, as there is a considerable number of demented patients with AD who have low numbers of neocortical NFT. It can be concluded that we still do not have definitive neuropathological criteria.

On the other hand, a crucial problem of premortal diagnosis is that the reliability of both clinical and neuroimaging methods is a function of disease severity, and therefore, there is a risk of increasing overlap with non-AD pathology, psychiatric illness and healthy aging (ICD-10, DSM-IV-TR, NINCDS-ADRDA), particularly in presence of comorbidities and cases of atypical AD syndromes, such as anterior (frontotemporal) and posterior (parietotemporo-occipital) variants of AD, focal, lobar or gyral progressive degenerative syndromes *(van Gunten A. et al., Brain Res. Rev. 2006).* Moreover, the clinical spectrum of symptoms of these conditions more closely correspond to the functional anatomy of the affected brain areas than to the underlying pathology.

However, in the last several years it has been clearly established that cerebrospinal fluid (CSF) biomarkers, particularly phospho-tau proteins, demonstrate a considerable increase in predictive value over existing algorithms comprising clinical, neurophychological and imaging modalities *(Hampel H. et al., Arch. Gen. Psychiatry 2004, de Leon M.J. et al., J. Int. Med. 2004, Hansson O. et al., Lancet Neurol. 2006).* Consequently, the time has come to include CSF examination as a part of routine diagnostic workup for suspected AD in both clinical and neuropathological evaluation of a patient.

NEW ASPECTS IN BASIC RESEARCH OF ALZHEIMER'S DISEASE (OP-B-12)

FUNCTIONAL MOLECULAR PROFILING OF ALZHEIMER'S DISEASE AND DOWN'S SYNDROME

WISEMAN HARRIS L, Lockstone H[1], Wayland M[1], Swatton J[2], Faull RM[3], Holland A[4], Bahn S[1]

[1] *Institute of Biotechnology, University of Cambridge, Cambridge, UK*
[2] *Dept of Biochemistry, University of Cambridge, Cambridge, UK*
[3] *Faculty of Medical and Health Sciences, University of Auckland, New Zealand*
[4] *Dept of Psychiatry, University of Cambridge, Cambridge, UK*
ljwh@cam.ac.uk

Down syndrome (DS) is a common genetic disorder caused by trisomy of chromosome 21, which results in a broad and variable phenotype. The disorder is primarily characterised by cognitive and language dysfunction coupled with sensory and neuromotor deficits and a neuropathology primarily characterised by decreased brain size and weight, abnormal gyrification and neurogenesis. Although DS is classically characterised as a developmental disorder, numerous pathologies develop specifically in later life. In particular, all DS individuals develop the neuropathological hallmarks of AD in the form of senile plaques, neurofibrillary tangles and granulovacuolar bodies by the age of 40. Overexpression of the APP gene on chromosome 21 has been proposed as the central event leading to AD type pathology in DS, in keeping with the amyloid cascade hypothesis of AD. However, the overexpression of APP alone has been demonstrated to be insufficient for the development of AD pathology in trisomic individuals. Thus it is of particular interest to compare and contrast biological findings from adult DS individuals and non-DS AD sufferers in order to further elucidate the key mechanisms in the development of this pathology. In our laboratory we have carried out protein profiling of adult brain tissue from DS individuals and AD patients. In addition we have used whole genome microarray chips to examine the gene expression profile of both adult and fetal brain tissue of DS individuals, in order to dissect out the underlying mechanisms of the DS phenotype from those specific to late-onset pathology including AD. These data will be presented in detail and provide interesting novel findings and new research directions in the investigation of both AD and DS.

ORAL PRESENTATIONS

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE

OP-C-(1-17)

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WHAT WE CAN EXPECT OF CURRENT DRUG DEVELOPMENT IN ALZHEIMER'S DISEASE

BABIĆ T

i3 research Maidenhead, UK
tomislav.babic@i3research.com

Only a small percentage of patients with Alzheimer's disease benefit from current drug therapy and for only a relatively short time. This is not surprising as the goal of these drugs is to enhance existing cerebral function in Alzheimer patients and not to block the progression of cognitive decline. In contrast, immunotherapy is directed at clearing the neurotoxic amyloid beta peptide from the brain that directly or indirectly leads to cognitive decline in patients with Alzheimer's disease. The single trial of active immunization with the amyloid beta peptide provided suggestive evidence of a reduction in cerebral amyloid plaques and of stabilization in cognitive function of half the patients who developed good antibody responses to the amyloid beta peptide. However, 6% of actively immunized Alzheimer patients developed sterile meningoencephalitis that forced the cessation of the clinical trial. Passive immunotherapy in animal models of Alzheimer's disease has provided similar benefits comparable to those seen with active immunotherapy and has the potential of bein effective in the half of Alzheimer's disease patients who do not make a significant anti-amyloid beta peptide antibody response and without inducing T-cell-mediated encephalitis. Published studies of 5 patients with sporadic Alzheimer disease treated with intravenous immunoglobulin containing anti-amyloid beta peptide antibodies showed that amyloid beta peptide was mobilized from the brain and cognitive decline was interrupted. Further studies of passive immunotherapy are urgently required to confirm these observation

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (OP-C-02)

NEURODEGENERATIVE DEMENTIAS OTHER THAN ALZHEIMER'S DISEASE

DANEK A

Neurologische Klinik, University Hospital, LMU, Munich, Germany
danek@lmu.de

Molecular genetic discoveries as well as new neuropathological observations have taught us much about dementias of the non-Alzheimer-type. In addition, better clinical distinction has become possible with improvements in neuropsychological approaches and in evaluation of signs and symptoms. Does distinction of these supposedly unusual dementias have any consequence for medical practice?

I argue that it does. The more the treatment of dementia becomes causally oriented - and there is considerable expectation and hope, given e.g. the antibody approach ("vaccination") to Alzheimer´s disease - the more important will it become to distinguish variants of degenerative dementia while the patients are still alive, perhaps even with brain biopsies. A final aim are biological markers in CSF or blood.

Presently, we can only collect all data available from clinical presentation, neuropsychology, neuroimaging, blood, CSF and molecular genetics and try to piece them together in a complex puzzle.

Even the still incomplete picture of today may lead to selection of distinct treatment approaches. This is best illustrated by Lewy-body dementia (LBD). On post mortem, it is characterized by the presence of cortical Lewy-bodies (made up of α-synuclein) and hallucinations, falls and parkinsonian symptoms are the clinical hallmarks of LBD. Patients suffering from Lewy-body dementia are particularly sensitive to neuroleptics and thus an explicit diagnosis may avoid potentially life-threatening complications.

Fronto-temporal lobar atrophies occur in a not inconsiderable number of older demented patients (~10%). Because of some common histological features (ballooned cells, tau-inclusions) they are summarized pragmatically as "Pick complex". One subtype (frontotemporal dementia, FTD) is characterized by behavioral impairment that includes loss of tact, disinhibition and even criminal action. Memory is little affected. In summary, in dementia the application of a differential diagnostic approach is equally as crucial as it is in other parts of medicine: it will lead to selection of differential treatment. Some observational drug studies have already been performed in fronto-temporal lobar atrophies but now systematic approaches are badly needed for the management of the various variants of degenerative dementia.

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THE EFFECT OF NADH (ENADA) IN TREATMENT OF ALZHEIMER'S DISEASE

DEMARIN V[1], Storga-Tomić D[2], Kay G[3], Martinić Popović I[1], Bosnar Puretić M[1], Birkmayer JGD[4]

[1] *Department of Neurology, "Sestre milosrdnice" University Hospital, Zagreb, Croatia*
[2] *Institute for Medical Chemistry, University of Graz, Graz, Austria*
[3] *Department of Neurology, Georgetown University School of Medicine, Georgetown, Kentucky, USA*
[4] *Labor Birkmayer and MEDINFO Inc, Vienna, Austria*
vida.demarin@zg.t-com.hr

Aim. Considerable evidence exists of dopaminergic neurotransmitter system dysfunction and oxidative stress in pathogenesis of Alzheimer disease (AD). Nicotinamide adenine dinucleotide (NADH) is biologically identified as a cofactor necessary for a number of cellular actions, such as energy production, cell regulation and DNA repair and repair of oxidative damage. The level of NADH is reduced in patients with neurodegenerative disorders. Clinical trials NADH has been shown to improve functioning in patients with Parkinson's disease and in chronic fatigue syndrome. The aim of the study was to establish weather NADH would improve cognitive functioning in patients with AD.

Methods. This was randomized, double blind, placebo-controlled study which included 48 patients with mild to moderate AD. Primary outcome measure was the difference in Mattis Dementia Rating Scale total score between baseline and after six months of treatment. The rest of cognitive tests included Hopkins verbal learning test, Fuld object memory test, Matching to sample test, Verbal fluency test, Clinical dementia rating scale and Mini Mental Status Scale Exam.

Results. NADH subjects improved significantly compared to placebo group in verbal fluency test. Placebo group experienced decrease of verbal fluency for 0.5 fewer words per minute and NADH group showed improvement of verbal fluency for 3.5 more words per minute ($p=0.056$). Six months after baseline a mean increase in MDRS Total score for NADH group was 2.8 (+/- 1.76) and for placebo group a mean decrease in MDRS Total score -4.9 (+/- 3.13) points ($p=0.022$).

Conclusions. The results from this trial consistently demonstrate benefit of stabilized oral NADH on cognitive functioning in AD patients.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (OP-C-04)

DEVELOPMENT OF QIS FOR THE MCS IN THE NETHERLANDS

DRAŠKOVIĆ I[1], Vernooij-Dassen M[1], Verhey F[2], Scheltens Ph[3], Olde Rikkert M[1]

[1]*Alzheimer Centre Nijmegen/WOK, Nijmegen, Netherlands*
[2]*Alzheimer Center Limburg, Maastricht, Netherlands*
[3]*Alzheimer Center VUmc, Amsterdam, Netherlands*
I.Draskovic@kwazo.umcn.nl

Objective: Diagnostic work-up, initiation, and monitoring of treatment probably is most effective and efficient in multidisciplinary MCs (MC's). However, there are insufficient data on the quality of care and the implementation rate of the latest dementia guidelines in MC's. To develop a set of valid, feasible and applicable QIs (QIs) for the MCs in the Netherlands based on the most recent Dutch Dementia guideline.

Methods: Participants. 18 MC;s took part in the study and were representative with respect to size, region and type (academic vs. non-academic hospitals) for the 36 MC's contacted. Besides experts from these MC's, informal caregivers and general practitioners (GPs) participated in postal rounds and panel discussions.

Procedure. To insure content validity, the indicators were based on the most recent 2005 Dutch Dementia guideline, and on recent studies on quality of care in dementia (ACOVE-project). To assess feasibility of application and measurement, importance, discriminative value, face validity, and concurrent validity of the indicators, RAND modified Delphi method was used including a postal survey round and several panel discussions. Face validity was assessed in a postal survey on an 8-points rating scale (1 = very low, 8 = very high validity). Applicability, feasibility of measurement and concurrent validity were assessed by analyzing a random sample of medical records (N =100, from10 MC's).

Results: The initial set of 56 single QIs was reduced to a final set of 14 indicators (8 complex, 6 single item), measuring quality of process, structure and outcome. Overall face validity was judged high, without significant differences between the expert panels (specialists, GPs). Indicators on outcome showed significantly lower face validity scores compared to process and structure indicators. QIs were able to discriminate between MC's: 2 out of 10 showed significantly lower percentage of adherence to the indicators than the rest.

Conclusion: The final QIs met the following metric requirements: content validity, face validity (quantified), internal consistency, inter-rater reliability, importance, feasibility of measurement, and application and concurrent validity. These 14 QIs were acceptable for a broad range of users, and were able to discriminate in quality between MCs.

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CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (OP-C-05)

CROATIAN THERAPEUTIC ALGORITHM FOR TREATMENT OF ALZHEIMER DISEASE

FOLNEGOVIĆ-ŠMALC V[1,2], Mimica N[1,2], Makarić G[1], Varda R[1], Silić A[3]

[1] *University Department of Psychiatry, Psychiatric Hospital Vrapče, Zagreb, Croatia*
[2] *School of Medicine, University of Zagreb, Zagreb, Croatia*
[2] *Psychiatric Hospital "Sveti Ivan", Zagreb, Croatia*
klinika@bolnica-vrapce.hr

Croatian professionals have not so far produced their own therapeutic algorithm predominantly due to administrative-material reasons. Practical meaning of a/m is that positive reimbursement list of HZZO does not name not a single drug for treatment of Alzheimer disease and purchase power of average Croatian patient suffering from Alzheimer disease is already compromised and extremely low. Local situation definitely does not represent an excuse, nevertheless it is our obligation to help physicians that are involved in treatment of patients suffering from Alzheimer disease by making Professionally drawn, well argumented Algorithm. Such Algorithm will represent additional motivation for HZZO.

Through and with Croatian Society for Clinical Psychiatry we will draw a proposal for Croatian Therapeutic Algorithm for Treatment of Alzheimer disease as well as implement education about drugs available in the therapeutic area with consequent intensification of requests on HZZO for at least partial reimbursement.

While making a/m Algorithm we will off course consult international currently used Algorithms as well as most recent literature on the subject.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (OP-C-06)

DEMENTIA AND ORGANIC PSYCHOSYNDROME IN ZADAR IN THE LAST 20 YEARS

GILIĆ A, Perinčić R, Kovač I

Zadar General Hospital, Zadar, Croatia
ante.gilic@zd.t-com.hr

According to the WHO report on the state of mental health published in 2001 the prevalence of Alzheimer's disease and other dementias is 0,6% in general population.

Zadar county has 165 000 inhabitants so using this percent we can predict there are some 1000 patients with Alzheimer's disease and dementia in our county.

We have investigated the rate of hospitalization of patients with Alzheimer's disease, other dementias and organic psychosyndrome in Psychiatric ward of General Hospital Zadar in the last 20 years. We divided this period in two parts - 1986 to 1995 (5 years before the war and 5 years of war) and 1996-2005 (ten years after the war).

We have found that the number of hospitalized patients with Alzheimer's disease, other dementias and organic psychosyndrome in 1986-1995 was:

Mb Alzheimer	Other dementia	organic psychosyndrome	Total
2	40	89	131

and the total number of hospitalized patients was 4439.

In the period of 1996-2005 the number of hospitalized patients with the same disorders was:

Mb Alzheimer	Other dementias	organic psychosyndrome	Total
54	136	138	348

and the total number of hospitalized patients was 6071.

We can see that in the first monitored period 2.64% of hospitalized patients had Mb Alzheimer, other dementias and organic psycho syndrome, and in the period 5.73% of the hospitalized patients had these disorders. The difference is statistically significant.

This difference can be interpreted in different ways -as the rise of total number of dementia and organic psychosyndrome patients in this area that results in the increased number of hospitalizations or as the decrease of family tolerance towards such patients and the wish for hospitalization.

In any case the society and psychiatric professionals are confronting a problem of increased pressure to hospitalize the patient with dementia or organic psychosyndrome, and as a society we have to take steps to adequately solve this emerging problem.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (OP-C-09)

ADVANCES IN EPIDEMIOLOGY OF DEMENTIA

HENIGSBERG N

Psychiatric Hospital Vrapče, Croatian Institute for Brain Research, Medical School, University of Zagreb, Zagreb, Croatia
neven.henigsberg@zg.t-com.hr

It is established by number of studies that prevalence of dementia sharply rises after 65 years of age, peaking over 20% in population over 85 years. However, there are considerable differences in observed prevalence rates across major surveys, and reported incidences by dementia types differ considerably between studies. A portion of observed differences could be explained by disparities in demographic characteristics of population in study, by differences in diagnostic instruments applied and by diversities in incidence rates between geographic areas.

Dementia in Alzheimer's disease and vascular dementia were predominantly studied in past decades, but recent studies shown that other types of dementia are of highest prevalence then previously believed, especially Lewy body dementia. New surveys also displayed that there is considerable overlap between dementia types. Incidence of mild cognitive impairment, now accepted as the separate entity that may, or may not, progress to dementia, is also significantly higher than previously believed.

A number of genetic and environmental factors were hypothesized to play a role in dementia onset. There is clear evidence that vascular dementia shares the same risk factors with cardiovascular and other cerebrovascular disorders. While in Alzheimer's dementia the role of genetic factor is clear, isolation of environmental factors is more difficult, frequently resulting in conflicting findings between studies. For other types of dementia clear insight in interplay of genetic and environmental factors is also missing.

Advances in neuroimaging is contributing to more specific and sensitive identification of dementia types in *in vivo* studies, providing more view on incidence and prevalence of dementia. Based on the fact that first symptoms are observable significantly before the diagnosis of dementia, long-term follow-up epidemiological studies are warranted to elucidate the real frequency and course of disorder.

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CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (OP-C-07)

DEVELOPMENT OF PSYCHOGERIATRICS IN CROATIA VIEWED THROUGH VALIDATION OF WORK WITH ALZHEIMER'S DISEASE PATIENTS

JUKIĆ V

Psychiatric Hospital Vrapče, Zagreb, Croatia
vlado.jukic@bolnica-vrapce.hr

Number of people aged 65 and beyond exceeded 15 % of total population several years ago. Such a relatively large number of elderly people means an increase in number of persons with mental problems, particularly those with Alzheimer's dementia. Such patients demand an adequate psychiatric care. Due to characteristics of mental disorders in elderly, a comparatively common psychotic decompensation in particular, they often need intensive hospital psychiatric treatment. Such treatment can only be organised and applied in psychiatric institutions. It would be best if separate psychogeriatrics wards were established in psychiatric hospitals.

A psychogeriatrics ward of the Psychiatric Hospital Vrapče, Zagreb was established more than fifty years ago, when population aged 65 and over accounted for much less than 10 percent in total population. An "extra bed" has always been asked for since. The available twenty beds are not enough and initiatives, substantiated with firm indicators, have constantly been pushed to increase the number of psychogeriatrics beds.

However, no psychiatric institution, including the Vrapče Hospital, has either responsibility or capacities to expand service without the support of the community. (Clearly, development of the psychogeriatrics as a professional and scientific field is a task performed by the professionals working in the relevant institutions.). And what is the "greater community" doing? Although it declaratively understands the need for more investment and expanding of the psychogeriatrics activities, nothing has materialized in practice. Moreover, attitude of the community towards psychogeriatrics viewed through the treatment of the AD patients indicates that there is no interest in development of this highly relevant field of psychiatry.

For illustration: Until recently (2002), psychogeriatrics (classified under geriatrics) was validated separately and the psychogeriatrics ward of the Psychiatric Hospital Vrapče had positive financial results. Since 2002, the psychogeriatrics patients have been validated as chronic psychiatric patients, and a highly demanding and intensive work on the ward has been inadequately paid. The Psychogeriatrics Service, which includes six intensive and seven acute psychiatric beds, is suffering losses. The losses have gradually increased

(from HRK 264,315 in 2002 to HRK 3,700,062 in 2005). What should a psychiatric institution do under such circumstances? Eliminate psychogeriatrics beds (which officially do not exist in administrative classification) and focus on less demanding and "cheaper" chronic psychiatric patients which do not cause operational losses for the Hospital?

We believe that the current situation is not permanent and expect that the authorities responsible for funding of hospitals will show consideration for actual needs, so the Vrapče Hospital decided not only to maintain but also to intensify work of its psychogeriatrics service. Closing down of a service which is currently not profitable would result in stagnation and lagging behind of psychogeriatrics as a profession. And we are responsible for the profession. The psychiatrists, which still run the psychiatric hospitals in Croatia, are responsible for development of the profession.

Thus, it might be said that there is no money but it must not be said that there is no need for psychogeriatrics beds and wards.

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CLINICAL DIFFERENTIATION BETWEEN ALZHEIMER'S AND FRONTOTEMPORAL DEMENTIA

LIŠČIĆ R

Institute for Medical Research and Occupational Health, Zagreb, Croatia and Alzheimer's Disease Research Center (ADRC), School of Medicine, Washington University, St. Louis, MO, USA
rliscic@imi.hr

Aim: The clinical diagnosis of Alzheimer's disease (AD) is now reliant on the use of the National Institute of Neurological and Communicative Disorders and Stroke and AD and Related Disorders Association (NINCDS-ADRDA)1 criteria. Other diseases causing dementia, for example frontotemporal dementia, are being increasingly recognized. A proportion of patients who meet clinical criteria for AD have frontotemporal lobar degeneration (FTLD) confirmed at autopsy with or without neuropathological AD-type changes. Thus, more sensitive clinical diagnostic tools, including psychometric tests, are required to distinguish between these pathological phenotypes at initial presentation, considering that AD and FTLD have different prognoses and treatment.

Methods: A retrospective review of 48 neuropathologically confirmed cases of FTLD according to clinicopathological consensus criteria of McKhann2 (70.6±9.5 years; 27 had completed psychometric testing) yielded clinical and neuropsychological features for comparison with 27 age-, sex-, education-, and severity- matched individuals with AD. Neary3 clinical consensus criteria for FTLD were used and a standard battery of psychometric tests was administered.

Results: At first visit, those with FTLD demonstrated more disinhibition and impulsivity ($p=0.0004$, Fischer's exact test), and less withdrawal ($p=0.01$) than those with AD. They also had more dysfluency ($p=0.01$), agrammatism ($p=0.004$), and speech hesitancy ($p=0.03$). The two clinical phenotypes had comparable executive dysfunction ($p=0.33$), but the AD group had more memory complaints ($p=0.01$). The FTLD individuals performed better than those with AD on a visual test of episodic memory but worse on word fluency ($p<0.05$) (performance correlated with aphasic features). 11/48 cases had additional AD-type pathology.

Conclusion: Clinical and cognitive features of FTLD may overlap with AD, particularly for memory and executive function, although behavioral problems and language difficulties distinguish those with FTLD. Psychometric tests help distinguish FTLD from AD, especially word fluency task, sensitive to frontal lobe dysfunction. Compounding the overlap of FTLD and AD clini-

cal phenotypes is the presence of AD-type pathology in one-fourth of FTLD individuals.

REFERENCES:

1. McKhann GM et al. Neurology. 1984;34:939-944.
2. McKhann GM et al. Arch Neurol. 2001;58:1803-1809.
3. Neary D et al. Neurology. 1998;51:1546-1554.

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CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (OP-C-11)

THE CLINICAL DILEMMA BETWEEN NORMAL AGING AND AGE CONDITIONED PSYCHICAL DIFFERENCES IN RELATION TO DEMENTIA

MAKARIĆ G

University Department of Psychiatry, Psychiatric Hospital Vrapce, Zagreb, Croatia
gordan.makaric@bolnica-vrapce.hr

All epdiemiological studies show, without any doubt, that older population grows faster than the rest of the population, by 2.4% per year. This is, among other things, definetly caused by the improvement of the life conditions, the style and type of nutrition, new and efficient possibilities for medical treatment of different illnesses. The part of older generation in total population will become 22% in 2030. As we take into account above data it is obvious the differentiation betwen the normal aging psychical changes, than the one caused by the illnesses and disorder in mental functions. The application of contemporary methods in diaganostics, and the detection of the early phases of the illness, and the distinction between psychical changes in the normal aging has one of the most important meaning for the predictive possibility of the prognosis of the treatment response. The aim of this work is to outline the difference between normal aging and excpected disorders in behaviour and the one caused by the development of dementia, which I would like to stress, is going to be in the future, one of the major public health problem.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (OP-C-12)

INVOLUNTARY EMOTIONAL EXPRESSION DISORDER IN DEMENTIA

MIMICA N[1], Presečki P[2], Mimica Ne[3]

[1] *Psychiatric Hospital Vrapče, University Department of Psychiatry, Zagreb, Croatia*
[2] *General Hospital Pula, Department of Psychiatry, Pula, Croatia*
[3] *Croatian Institute for Health Insurance, Zagreb, Croatia*
ninoslav.mimica@bolnica-vrapce.hr

Involuntary emotional expression disorder (IEED) is proposed to describe a syndrome of relatively stereotypical episodes of uncontrollable crying and/or laughing, resulting from lesions of multiple types, in multiple brain regions. Episodes may be incongruent with mood or congruent with mood, but excessive. A number of patients suffer from this unique syndrome, including individuals who have suffered a stroke or traumatic brain injuri (TBI) as well as patients with amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), dementias such as Alzheimer's disease, and motor disorders such as Parkinson's disease. This suggest a common emotional neurobiological substrate for IEED (frontal - subcortical - cerebellar networks), disrupted in the diseases in which IEED occurs. IEED is underrecognized by clinicians, misdiagnosed and undertreated.

Distinguishing IEED from mood disorders and other behavioral disturbances is imperative given that the treatments for these conditions are not identical. Rating scales can assist in quantifying the severity of IEED, but are not used in diagnosis.They should be applied after the presence of the syndrome has been estabilished using the draft criteria.There are at least 2 scales that may be of use toward this end: the Pathological Laughter and Crying Scale (PLACS) and the Center for Neurologic Study - Lability Scale (CNS-LS).

Pharmacological treatment can reduce symptoms and improve quality of life for the patient. Small-scale studies suggest that tricyclics (TCAs) and selective serotonin uptake inhibitors (SSRIs) may improve IEED symptoms. Two large, double blind studies have shown that dextromethorphan (DM) and quinidine (Q) is an effective treatment for IEED. No evidence for benefit of nonpharmacological approaches on number of crying/laughing episodes.

This presentation will review the nosology, clinical phenomenology, differential diagnosis, and evaluation methods relevant to the identification and treatment of IEED in the clinical practice of psychiatry.

References:
1. Schiffer RB, Pope LE. J Neuropsychiatry Clin Neurosci 2005;17:447-54.
2. Lauterbach EC. Neurology 1994;44:983-4.
3. Burns A, et al. Int J Geriatr Psychiatry 1999;14:681-5.
4. Brooks BR, et al. Neurology 2004;63:1364-70.
5. Robinson RG, et al. Am J Psychiatry 1993;150:286-93.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (OP-C-08)

OVERVIEW OF THE FIRST FIVE CONSENSUS STATEMENTS FOR IMPROVEMENT OF QUALITY OF DEMENTIA CARE ACROSS EUROPE

OLDE RIKKERT M[1], Burns A[2], Robert P[3], Selmes J[4], Stoppe G[5], Waldemar G[6], Sartorius N[7]

[1] *Department of Geriatrics/Alzheimer Centre Nijmegen, University Medical Centre Nijmegen, The Netherlands*
[2] *Dept Psychiatry, School of Psychiatry and Behavioural Sciences, University of Manchester, United Kingdom*
[3] *Centre Memoire de Ressources et de Recherche, CHU de Nice, Nice, France*
[4] *Madriaga Foundation, Brsusel/EDCON secretary general*
[5] *Dept of Psychiatry, University Hospital Basel, Switzerland*
[6] *Memory Disorder Research Unit, Department of Neurology, Neuroscience Centre, Copenhagen University Hospital Rigshospitalet, Denmark*
[7] *Dept of Psychiaty, University Hospital Geneva, Switzerland*
M.Olde-Rikkert@ger.umcn.nl

Introduction: Dementia has far-reaching implications for patients and their primary caregivers and currently is a major driver of costs in health care and social systems across Europe. Many issues relating to the care and treatment of people affected by dementia remain controversial and unresolved.

EDCON is a network of European experts in the field of dementia, which identifies and builds consensus on controversial issues relating to this disease area, with the aim to improve the quality of life of those affected, as well as their caregivers.

Methods: EDCON is managed by a Steering Committee, consisting of dementia experts, which identifies controversial issues relating to dementia and selects topics around which consensus needs to be built. This Committee defines strategies and methodologies, and sets up expert working groups to develop and agree 'consensus statements', which are then being sent out to third party organisations for endorsement and wider dissemination.

Results: So far EDCON established 5 consensus statements, which consecutively are addressing:

- Disclosure of dementia diagnosis to the patient
- Improving standards of dementia care
- Access to diagnostic evaluation and medical treatment for dementia
- Competence in dementia
- Ethics of genetic research in dementia

Two consensus statements, concerning outcome measures in dementia and controversies in prevention are in preparation.

Discussion: In this conference an outline of the first five consensus statements will be given, focussing also on practical consequences for dementia care. With regard to the access to cholinesterase inhibitors recent data on the heterogeneity of prescription and reimbursement across Europe are shown.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (OP-C-13)

IMAGING DEMENTIA

SCHMIDT R

Department of Neurology, Medical University Graz, Graz, Austria
reinhold.schmidt@meduni-graz

Aim: Description of the opportunities of neuroimaging methods in the diagnosis of dementia

Methods: The presentation will provide video sequences of the clinical presentation of patients with various types of dementia and demonstrate respective imaging results to demonstrate the impact of morphological and functional techniques in daily clinical practice.

Results: For the diagnosis of Alzheimer disease it will be shown that progression of disease can be followed by MRI and volumetrics are helpful in differential diagnosis. MRI and PET are also promising tools in monitoring treatment response to Alzheimer´s disease. MRI is particularly suited to demonstrate putative neuroprotective effects of treatment. For vascular dementia there exist problems in defining the type of lesions related to a vascular dementia syndrome and operationalization of current imaging criteria is need to obtain acceptable inter-rater agreement. As will be shown in case studies morphological and functional imaging is an important adjunct in the diagnosis of rare causes of dementia such as frontotemporal degeneration, posterior cortical atrophy or Creutzfeldt Jakob disease.

Conclusion: Morphological methods are mandatory in dementia diagnosis, functional methods can be supportive in many cases particularly in early disease stages and both modalities hold promise to be used as surrogate markers in treatment trials.

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HOSPITAL MORBIDITY OF ALZHEIMER'S DISEASE IN CROATIA

SILOBRČIĆ RADIĆ M, Hrabak-Zerjavić V

Croatian National Institute of Public Health, Zagreb, Croatia
maja.silobrcic-radic@hzjz.hr

Aim: To present Alzheimer's disease hospitalisation trends in Croatia during the 1995-2004 period and to point out the problems that appear with the registration of this disease.

Methods: Epidemiological analysis has been based on inpatient statistical data for Alzheimer's disease/dementia (G30/F00*) and Delirium not induced by psychoactive substances/delirium superimposed on dementia (F05/F05.1). The presentation shows absolute figures, crude and specific rates per 100,000.

Results: Alzheimer's disease has been introduced as a separate diagnostic category with the ICD 10. It was probably the reason for recording fewer hospitalisations in 1995 and 1996 (38, respectively 35). In 1997, there were 204 hospitalisations (rate 4.3). Both the number and the rate of hospitalisations kept oscillating. The largest number of hospitalisations was recorded in 2001 and 2004 (308, rate 6.9; 302, rate 6.8; male 4.2, female 9.2). The average length of hospital care in 2004 was 44.9 days. In 1995, 229 hospitalisations for the Delirium superimposed on dementia were recorded. The following year, the number and the rate doubled. Over the period 1999 2003 a rising trend in the hospitalisation was evident (414, rate 8.7 in 1999; 674, rate 15.2 in 2003). In 2004, the reported hospitalisations numbered 578 (rate 13.0; male 10.0, female 15.8). The average length of hospitalisation was 44.8 days. Whereas more than 80% hospitalisations for Alzheimer's disease occurred over 65 years, more than 90% of those for Delirium superimposed on dementia did. In both diagnoses, hospitalisation rates showed a marked increase through to the oldest age.

Conclusion: Since under WHO rules, Dementia in Alzheimer's disease (F00*) may not be recorded as a separate diagnostic category, it has to be linked with the Alzheimer's disease code (G30). Some of these dementias stay hidden under the main discharge diagnosis of Delirium superimposed on dementia (F05.1). In routine recording, a certain number of Alzheimer's dementia cases are thereby lost. One should also assume that no small number of Alzheimer's dementia get diagnosed as Organic psychosyndrome, and some as Unspecified dementia. Continuous training relating to proper coding and recording is necessary to ensure the optimal epidemiological monitoring of Alzheimer's disease.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (OP-C-15)

LEGAL ASPECTS OF DEMENTIA ASSESSMENT EXPERTISE

ŠERIĆ V, Jurašić MJ, Demarin V

"*Sestre milosrdnice*" *University Hospital, Department of Neurology, Zagreb, Croatia*
mkesic@inet.hr

Judicial and medical care systems are two different scientific disciplines with different sets of knowledge and approach to the same problem: understanding the human being and behavior in the interest of just approach to his actions.

Social, legal and moral norms regulate relationships and coexistence in a community.

In most countries increase in elderly criminality has been observed, still low in figures compared to that of younger perpetrators.

According to some indicators elderly criminality is hard to prove implying the existence of "dark figures".

Some criminologists believe that "dark figures" of elderly criminality show strong public emotions that legal punishment is not the proper mean of treatment of the elderly and feeble persons.

Thus legal norms do not explicitly address the elderly and their older age changes opposed to underage delinquency that constitutes separate legal status.

The law does allow acknowledgment of phenomenological and etiological specificities of criminal acts performed by the elderly implying weaker punishment, individual approach and adjustment to specificities and differences of such age.

Frequently daily judicial problem is: what to do with the elderly delinquents? During the expertise process it is important to determine if aging is physiological or if dementia has begun. In case of dementia, specific type and cause, course and prognosis need to be assessed with special insight into how important is the influence of social factors in a delinquent act. Alcohol abuse and some other influences cannot be overseen. These people are then labeled as partially or completely wayward. If greater criminal act has been performed or if there is social danger it is necessary to think of safety issues and proper medical treatment with institutionalized medical care.

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CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (OP-C-16)

DEMENTIA: DIAGNOSIS VS. SYMPTOM AND FUNCTIONING ASSESSMENT - CLINICAL TOOLS

ŠTRUKELJ KB, Groleger U, Kogoj A

University Psychiatric Hospital Ljubljana, Ljubljana, Slovenia
katarina.strukelj@psih-klinika.si

The needs of people with dementia and their relatives exceeds greatly the capacities of any mental health service as complex and organized as it might be. Confirming the diagnosis of dementia is an essential step in the following treatments and help, but is nevertheless not enough. The group of patients with dementia is a heterogenous group with diferent symptoms, course, response to treatment, additional medical, behavioural and psychological symptoms, needs, functioning and levels of support needed. The routine everyday psychiatric practice seldom covers the majority of these issues. For that reason a complex, multidisciplinary, secondary psychiatric service was introduced for the elderly with psychiatric disorders at University Psychiatric Hospital in Ljubljana. As a part of routine assessment and follow-up as comprehensive protocol was introduced. In the present study we are interested in the role of different clinical measures in a complex assessment of patients with dementia. The data will be presented for patients within the same diagnostic groups of different dementias. The data will confirm, that the diagnosis itself is not enough to follow-up patients and their families properly; that the treatment might be tailored more efficiently; that the prognosis is easier to predict and that the meeds of patients is easier to assess and tailor the non-medical help strategies. Although psychiatrists stay reluctant to use clinical measures in their everyday work, our data will confirm, that the quality of work with the elderly and especially elderly with dementia, improves significantly. For conclusions we will propose the essential parts of a standardized outpatient protocol for patients with dementia.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (OP-C-17)

REGISTRY OF ALZHEIMER'S DISEASE PATIENTS AND OTHER ELDERLY PATIENTS WITH MENTAL DISORDERS (CROATIA, 2003-2005)

TOMEK-ROKSANDIĆ S[1], Puljak A[1], Ivanda T[2], Mihok D[1], Perko G[1], Radašević H[1], Vidas-Kaćanski A[3], Kovač M[4], Pecotić Z[5], Čulig J[1]

[1] *Centre for Gerontology of the Zagreb Public Health Institute - Ministry of Health and Social Welfare Reference Centre for Health Protection of Elderly People, Zagreb, Croatia*
[2] *Ministry of Health and Social Welfare of the Republic of Croatia, Zagreb, Croatia*
[3] *Rab Psychiatric Hospital, Rab, Croatia*
[4] *"Dr. Ivan Barbot" Neuropsychiatric Hospital, Popovača, Croatia*
[5] *Psychiatric Hospital Vrapče, Zagreb, Croatia*
gerontologija@publichealth-zagreb.hr

Increase in prevalence of dementia intensifies with age. The prevalence of Alzheimer's disease doubles every 5 years beyond age 60. One in twelve people older than 65 has Alzheimer's disease, and 24% of all people aged 75 and older are affected by some form of this disease. In developed countries, namely in countries with "old population" (including Croatia), nearly 50% of population aged 85 and older have Alzheimer's disease. The futurology envisages, when it comes to gerontology, that growth in population aged 85 and beyond shall result in one in three persons being affected by Alzheimer's disease, so its early detection and registration for geroprophylaxis and treatment is imperative. Therefore, it is necessary to set up and maintain the Croatian Registry of Alzheimer's Disease Patients and Other Patients with Mental Disorders, which is a task assumed by gerontology as a public health service.

For more information visit www.publichealth-zagreb.hr

REFERENCES:

1. Tomek-Roksandić S, Perko G, Lamer V, Tomić B, Čulig J, Kramarić D, Pecotić Z: Uzroci hospitalizacije i mortaliteta psihogerijatrijskih bolesnika u Zagrebu i po županijama Hrvatske. Medix 2002;43:105-108.
2. Tomek-Roksandić S, Perko G, Mihok D, Radašević H, Čulig J: Risikofaktoren des ungesunden Alterns. Acta Medica Austriaca 2003;30(Suppl 1):8-9.
3. Tomek Roksandić S, Perko G, Mihok D, Puljak A, Radašević H, Ljubičić M: Nepokretnost, nesamostalnost, nestabilnost i nekontrolirano mokrenje. "4 N" u gerijatriji. Medix 2005;58:108-113.

4. Tomek-Roksandić S, Perko G, Mihok D, Puljak A, Radašević H, Čulig J, Ljubičić M: Značenje Centara za gerontologiju županijskih zavoda za javno zdravstvo i Gerontoloških centara u Hrvatskoj. Medicus 2006; 2:195-203.

5. Tomek-Roksandić S, Perko G, Puljak A, Mihok D, Radašević H, Ljubičić M: Health Management for Elderly in the Function of the Croatian Economy Growth. Liječnički vjesnik 2006;128(Suppl 1):28-30.

ORAL PRESENTATIONS

CURRENT TRENDS IN ORGANIZATION OF SELF-HELP GROUPS AND CARE-GIVERS EDUCATION

OP-G-(01-02)

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CURRENT TRENDS IN ORGANIZATION OF SELF-HELP GROUPS AND CARE-GIVERS EDUCATION (OP-G-01)

ALZHEIMER'S DISEASE: A PRESENTATION FOR THE NON-EXPERTS

DIAMOND J

Alzheimer Society of Canada, Toronto, Canada
jdiamond@alzheimer.ca

What is Alzheimer Disease, and how is it diagnosed?

What are "risk factors", and how can they be reduced?

What are "genetic" risk factors?

What is the significance of Mild Cognitive Impairment (MCI)?

What are "Plaques and Tangles" and why are they dangerous?

The drugs we have now; how they work, and their limitations.

The next ten years: earlier diagnosis and new treatments that attack the disease.

Promoting brain repair, and the role of the caregiver.

CURRENT TRENDS IN ORGANIZATION OF SELF-HELP GROUPS AND CARE-GIVERS EDUCATION (OP-G-02)

ADI - PAST, PRESENT AND FUTURE

McGREGOR C

Alzheimer Scotland - Action on Dementia, Edinburgh, Scotland
cetsm@dircon.co.uk

Alzheimer Disease International (ADI) is a worldwide federation of Alzheimer

associations. Established in 1984 ADI is an organisation aiming to unite people concerned with dementia throughout the world. From small beginnings ADI now works with Alzheimer associations in 75 different countries to support people with dementia and their families.

Through its activities and support, ADI aims to improve the quality of life for people with dementia and their carers, to raise global awareness of the disease, encourage the sharing of information, experience and good practice and to promote advances in research and dementia care.

This address will describe the work of ADI with particular emphasis on current and

planned activities. As 2006 marks 100 years since Alzheimer's disease was first diagnosed, there are currently 24 million people with dementia worldwide this presentation will also highlight the benefits of being part of the world movement facing the ongoing challenges of the increased prevalence of dementia.

POSTER PRESENTATIONS

NEW ASPECTS IN BASIC RESEARCH OF ALZHEIMER'S DISEASE

PP-B-(01-05)

3rd Croatian Congress on Alzheimer's Disease with international participation
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CEREBROSPINAL FLUID LEVELS OF TOTAL TAU PROTEIN, TAU PROTEIN PHOSPHORYLATED AT THREONINE 181 AND 199 AS MARKERS FOR EARLY-ONSET ALZHEIMER DEMENTIA

BOBAN Ma[1], Grbic K[2], Hof PR[3], Hamann C[4], Ackl N[4], Bader B[5], Danek A[4], Šimić G[2]

[1] *Clinical Hospital Center Zagreb, Department of Neurology, Medical School University of Zagreb, Zagreb, Croatia*
[2] *Croatian Institute for Brain Research, Zagreb, Croatia*
[3] *Mount Sinai School of Medicine, New York, USA*
[4] *Neurologische Klinik, Klinikum der Universität München, München, Germany*
[5] *Zentrum für Neuropathologie und Prionforschung, Ludwig-Maximilians-Universität München, München, Germany*
maboban@mef.hr

Background: Abnormal hyperphosphorylation of the microtubule-associated protein tau and its incorporation into neurofibrillary tangles are major hallmarks of the pathogenesis of Alzheimer's disease (AD). The cerebrospinal fluid (CSF) levels of phosphorylated tau proteins reflect the phosphorylation state of tau in the brain. Using monoclonal antibodies, different tau phosphoepitopes can be sensitively detected in CSF.

Objective: To determine the diagnostic value of CSF total tau protein (t-tau), tau protein phosphorylated at threonine 181 and 199 (p-tau181 and p-tau199) in early-onset AD versus healthy controls (HC) and other primary causes of dementia, such as frontotemporal dementia (FTD) and vascular dementia (VaD).

Patients and methods: Patients with clinical diagnosis of MCI (mild cognitive impairment), probable and possible AD, as well as FTD, VaD and HC were included in the study. CSF levels were measured using commercially available ELISA kits (t-tau and p-tau199 - BioSource, Camarillo, CA, USA and p-tau181 - Innogenetics, Ghent, Belgium).

Results: Mean CSF t-tau and CSF p-tau181 levels were significantly elevated in AD patients compared to FTD, VaD patients and HC. Additionally, in differentiation between AD versus FTD and VaD, CSF p-tau181 has shown best sensitivity and specificity.

Conclusion: Our results confirmed earlier findings that p-tau181 may be an useful, promising biological marker for distinguishing AD from other primary causes of dementia (FTD and VaD).

NEW ASPECTS IN BASIC RESEARCH OF ALZHEIMER'S DISEASE (PP-B-02)

PHOSPHORYLATED TAU EPITOPES THREONIN 231 AND THREONIN 181 IN THE EARLY DIAGNOSIS OF ALZHEIMER'S DISEASE

GRBIĆ K[1], Boban M[1], Hof PR[2], Hamann C[3], Ackl N[3], Bader B[4], Danek A[3], Šimić G[1]

[1] *Croatian Institute for Brain Research, Zagreb, Croatia*
[2] *Mount Sinai School of Medicine, New York, USA*
[3] *Neurologische Klinik, Klinikum der Universität München, München, Germany*
[4] *Zentrum für Neuropathologie und Prionforschung, Ludwig-Maximilians-Universität München, München, Germany*
kgrbic@hiim.hr

Abnormal hyperphosphorylation of the microtubule-associated protein tau and its incorporation into neurofibrillary tangles are major hallmarks of the pathogenesis of Alzheimer's disease (AD). Using monoclonal antibodies, different tau phosphoepitopes can be sensitively detected in the cerebrospinal fluid (CSF). A significant elevation in the levels of tau protein phosphorylated at threonine 231 (p-tau231) and threonine 181 (p-tau181) has been recently observed in CSF of AD patients (Hampel H et al., Arch Gen Psychiatry 2004; 61: 95-102; de Leon MJ et al., J Intern Med 2004; 256: 205-223).

We analyzed a group of patients with a clinical diagnosis of AD, with possible AD, and nondemented controls. CSF levels of p-tau231 were measured using a specific antibody against the 231 tau phosphoepitope by Western blot (using an antibody provided by Peter Davies, New York, USA). CSF levels of p-tau181 were measured by ELISA (Innotest Phospho-Tau (181P), Innogenetics, Ghent, Belgium).

CSF levels of p-tau231 and p-tau181 were significantly elevated in the patients with definite AD compared to the nondemented controls. Our preliminary results in a small group of cases with mild cognitive impairment (MCI) largely confirmed two earlier studies, which suggest that such an elevation may be a specific indicator of AD-related changes and could improve early detection and tracking disease progression. We conclude that p-tau231 and p-tau181 in CSF represent a promising potential biological markers of AD.

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NEW ASPECTS IN BASIC RESEARCH OF ALZHEIMER'S DISEASE (PP-B-03)

PHOSPHORYLATION OF TAU PROTEIN DURING EARLY DEVELOPMENT AND PROGRESSION OF ALZHEIMER'S DISEASE

JOVANOV-MILOŠEVIĆ N[1], Grbić K[1], Kostović I[1], Hof PR[2], Šimić G[1]

[1] *Croatian Institute for Brain Research, School of Medicine, Zagreb, Croatia*
[2] *Mount Sinai School of Medicine, New York, USA*
njovanov@hiim.hr

Background and Aim: Some of our previous findings suggested that abnormal hyperphosphorylation of tau protein in Alzheimer's disease (AD) may result from the reactivation of fetal plasticity mechanisms. However, the phosphorylation of tau protein in the fetal telencephalon remained poorly investigated. Therefore, the aim of this study was to examine the presence and distribution of AT8-immunoreactivity (AT8-ir) in the human brain during several stages of fetal development, and to compare with a normal elderly, mildly cognitively impaired (MCI) and AD brain.

Methods: The AT8 mouse monoclonal anti-human tau antibody (Innogenetics, Temse, Belgium) was employed in indirect-immunocytochemistry (dilution 1:200) and Western blot (dilution 1:500) on samples of thirteen fetal human brains, two adult control and two MCI, as well as ten AD cases. AT8 reacts with tau only when multiple sites around Ser202, including Ser199, Ser202 and Thr205, are phosphorylated. Single phosphorylation of any of the residues is not enough for AT8 reactivity. Thus, AT8-ir is useful in detecting phosphorylation of Ser202/Thr205 for proline-directed kinases. As shown by Braak and collaborators, AT8-ir permit the evaluation of neuronal changes well before the actual formation of neurofibrillary tangles and neuropil threads.

Results: Specific AT8-ir was found already at 10th week of gestation (w.g.), which was the earliest fetal stage examined. AT8-ir was most prominent in the lower subplate zone at about 18th w.g. and in the upper subplate around 20th w.g.; it then gradually diminished and disappeared to the end of 32nd w.g., implying that this phosphorylation of tau is most pronounced in a distal part of growing cortical afferents. During mid-gestation, the fornix as well as a subset of callosal commissural fibers were unambiguously AT8-ir, while the internal capsule remained unstained in this period, supporting the same suggestion. Unlike in control cases, in MCI brains many entorhinal and hippocampal neurons, as well as some neurons of the temporal isocortex, presented initial cytoskeletal changes such as AT8-ir tortuous varicose apical dendrites and curved, thickened dendrites. In these two cases, we have also found previously poorly described AT8-ir fibers in the transentorhinal/entorhinal cortex and hippocampal formation. Beaded- or rod-like AT8-ir was most con-

spicuous in the perforant fascicle and in CA1 axons projecting into the subiculum. In the AD brain AT8-immunoreactive neurons were characterized by coarse AT8-ir granules, but most tangle-bearing neurons were not AT8-ir.

Conclusions: The present work provides data on the normal developmental pattern of phosphorylation of tau protein in the fetal human brain. Results obtained in MCI and AD cases clearly show a layer- and stage-specific pattern of tau hyperphosphorylation during the progression of Alzheimer's disease. Since this AT8-ir is identical to that found in the fetal brain, we may conclude that some proline-directed kinases are abnormally reactivated during the early course of AD.

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PHOSPHORYLATION OF TAU PROTEINS IN DEVELOPMENT AND ALZHEIMER'S DISEASE

MLADINOV M[1], Boban M[1], Boban Ma[2], Grbić K[1], Mimica N[3], Šimić G[1]

[1] *Croatian Institute for Brain Research, Zagreb, Croatia*
[2] *Clinical Hospital Center Zagreb, Department of Naurology, Medical School University of Zagreb*
[3] *Psychiatric Hospital Vrapče, University Department of Psychiatry, Zagreb, Croatia*
gsimic@hiim.hr

Tau proteins belong to the microtubule-associated proteins (MAP) and are crucially involved in microtubule assembly, stabilization and cytoskeleton maintenance. Tau proteins also allow microtubules to interconnect with other cytoskeletal components and regulate their growing dynamics. The biological activity of tau is controlled mostly by phosphorylation and, to a lesser degree, by glycosylation. Phosphorylation of tau proteins is developmentally regulated. It is high in fetal period and decreases with age.

A single gene on the long arm of chromosome 17 encodes the human tau protein. Its primary transcript contains 13 exons. In adult human brain, six tau isoforms are expressed by alternative splicing of exons 2, 3 and 10. The isoforms length range from 352 to 441 aa. The unique expression pattern of tau isoforms in humans could represent a link to the particular vulnerability of humans to neurodegenerative disorders, particularly Alzheimer's disease (AD).

Brain neurodegenerative disorders characterized by intraneuronal and glial fibrillar lesions formed by tau proteins are known as tauopathies. Tau proteins from these lesions are abnormally phosphorylated, which is probably the most important cause of their aggregation.

There have been many attempts to find an accurate biomarker in the cerebrospinal fluid (CSF) for the diagnosis of neurodegenerative diseases. Phosphorylated tau as a marker for AD came closest to this aim. The main long-term goals of the project in our laboratory are: 1) to determine how abnormalities of the selected phospho-tau epitopes 181, 199, 202/205, 231, 396/404 and 422, ratio of 3R/4R tau isoforms and total tau in CSF, as revealed by enzyme-linked immunosorbent assay (ELISA), Western blot and eventually mass spectrometry, relate to alterations in glutamatergic transmission, MRI-determined entorhinal and hippocampal atrophy and cognitive changes; 2) to identify and evaluate the possible role of reactivated fetal kinases in the tau phosphorylation in AD and to test the presumed protective action of fetal tau isoform (which has only 3 microtubule binding domains - 3R) on tau polymerization in neuronal cell culture. Through fulfillment of these goals, we expect to obtain new knowledge relevant for tracking the progression of neurofibrillary degeneration and early detection of AD.

NEW ASPECTS IN BASIC RESEARCH OF ALZHEIMER'S DISEASE (PP-B-05)

CHARACTERISTIC MR SPECTROSCOPY METABOLITE PROFILES AND LOW PHOSPHO-TAU/TOTAL-TAU RATIO IN DIFFERENTIATING CREUTZFELDT-JAKOB DISEASE FROM ALZHEIMER'S DISEASE

ŠARAC H[1], Hajnšek S[2], Bašić S[2], Radoš M[1], Henigsberg N[1], Šimić G[1]

[1] *Croatian Institue for Brain Research, Diagnostic Center Neuron, Zagreb, Croatia*
[2] *University Hospital Center Zagreb, Department of Neurology, Zagreb, Croatia*
helanasarac@hi.t-com.hr

Sporadic Creutzfeldt-Jakob disease (sCJD) is characterised by progressive dementia, ataxia and myoclonus. As clinical signs may overlap with other dementing or neurodegenerative disease, other criteria are used in diagnosis of CJD. ELectroencephalogram (EEG) and 14-3-3 protein immunoassay in cerebrospinal fluid (CSF) are highly sensitive and specific diagnostic criteria for probable sCJD disease premortem. Hyperintensities in basal ganglia is common finding in CJD, but of questioned specificity and sensitivity.

Autopsy proven sporadic CJD presented by progressive dementia, ataxia and myoclonus is described. Negative 14-3-3 immunoassay along with non-specific initial EEG which disclosed a bihemispheric slowly high-voltage spiky waves had strongly supported an alternative diagnosis to CJD. MRI has shown mild cortical atrophy, diffuse high signal intensity over white matter, periventricular abnormality and mild cortical atrophy, diffuse high signal intensity of basal ganglia. MR spectroscopy (MRS) are conductive to massive neuronal death. Phospho-tau/total-tau ratio separated CJD from other dementing or neurodegenerative illnesses. Results of the postmortem neuropathologic analysis, along with immunohistochemical verification of the diagnosis by an European center are presented.

Described case suggest that rapidly progressive dementia with negative 14-3-3 test and non-specific initial EEG and MRI must still be considered in the differential diagnosis of sporadic CJD. By characteristic findings, we conclude that serial MRI and MRS studies in paralel phospho-tau/total-tau ratio is helpfull in differentiating CJD from other dementing illnesses.

POSTER PRESENTATIONS

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE

PP-C-(01-18)

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THE ROLE OF NEUROIMAGING METHODS AND TRANSCRANIAL COLOR DOPPLER (TCD) IN VASCULAR (VAD) AND ALZHEIMER DEMENTIA (AD)

BAŠIĆ KES V, Jurašić M, Vuković V, Lovrenčić Huzjan A, Demarin V

"*Sestre milosrdnice*" *University Hospital, Department of Neurology, Zagreb, Croatia*
kespetar@net.hr

Recent studies have shown the VaD and AD might overlap in certain pathophysiological aspects. The aim of this study was to evaluate the role of neuroimaging methods and TCD in diagnostics of different kinds of dementia.

Mean blood flow velocities (MBFV) were measured in right and left middle cerebral arteries (MCA) and in basilar artery (BA) in rest conditions by transcranial Doppler ultrasonography with a 2 MHz probe in two groups of patients: a) Alzheimer's disease (AD, N=43, age=72,79 +/-8 years), b) patients with vascular dementia (VaD, N=23, age=77,43 +/- 7).

The computerised tomography (CT) and magnetic resonance imaging (MRI) were performed in all patients.

The results of CT and MR showed atrophy in 35 AD and 17 VD patients, the signs of hypoperfusion in 19 AD and 13 VD patients. Three AD and 4 VD patients had ischemic lesions while lacunar changes were found in 5 AD and 8 VD patients.

No significant differences in MBFV measured by TCD have been detectable between patients with AD and VD.

TCD is convenient method for evaluation of intracerebral hemodynamic, however in settings of dementia. TCD has not shown to be reliable method for differentiation between Alzheimer and vascular type of dementia.

Due to a high prevalence of lacunar changes on CT and MR in both AD and VaD, current research in our laboratory is focused on the role of TCD emboli monitoring in pathophysiology of these types of dementia.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-02)

WHEN MORBUS ALZHEIMER?

DRAGAČ-PAIĆ V, Rajić-Valić D

Croatian Institute for Health Insurance, Zagreb, Croatia
bernard.kotlar@zd.t-com.hr

Aim: We tried to emphasize an early appearance of the mental disability and after that fast development of physical handicap of persons suffering from Alzheimer's disease who were taken care of and treated in the Psychiatric Hospital Ugljan. 90% of the cases were female patients, mostly without positive psychiatric heredity. Usually, the appearance was very notable, almost violent, with the loss of mental strength in the form of pre-senile dementia, that is, the irreversible diminishing of the intellectual freshness and independent functioning. When the disease was diagnosed the patients were between 50 and 60 years old. At the beginning of the disease, they were on so-called home family care and because of different reasons, by worsening of the clinical status, in the second and third year of disease the family couldn't take care of them, "cover them" or tolerate them nor be engaged in anymore (decompensation of family members).

Methods and Results: The average appearance in the second and third year od disease. Diagnostically, the big evidence of changed EEG can be seen: the occur-ence of diffused delta rhythm, that is, weak alpha rhythm. CT - cranium speaks generally about the diffused cortical atrophy.

We find out from the heteroanamnestic data that the patients were in good health in general, before the disease, they lived normal decent life, but the disease was preceded by some serious family problem, quarrel (stress), serious and exhausting illness, especially infective one (influenza, pneumonia), injury of locomotor apparatus (arm, leg or pelvis fracture) with the presence of intensive fear.

The hospitalization of patients with Alzheimer's disease was followed as the result of intellectual disintegration of patients, like pre-senile dementia, that is, memory damage, data learning problems, loss of orientation, verbal expression disturbance, appearance of the psycho motor agitation with hallucinations and physical exhaustion. The psychotic state was permanent, and it was gradually replaced by neurologic clinical status of pseudoparkinsonism and hypertonia-in the sense of complications during the treatment.

Conclusion: Pre-senile dementia is still non lethal (infaust) disease. Dramatically and very fast physical and psychic destruction show us the poor knowledge of the very aetiology of the disease and the treatment and we can say the prevention does not exist either. It can be characterized as malignant,

as in the end, in so-called terminal phase only care and appropriate medical treatment remain (because of final immobility of patient and the most often decubitus condition).

"..... because the man with dementia was deprived of the fortune he used to have..... (Eskirol)

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-04)

COGNITIVE DEFICITES IN ALZHEIMER'S DISEASE AND MORPHOLOGICAL SUPSTRATUM

JOSIPOVIĆ-JELIĆ Ž

Medikol Polyclinic, Zagreb, Croatia
zeljka.josipovic-jelic@si.htnet.hr

It is necessary to know anatomy and pathology of mental processes to understand cognitive changes of Alzheimer dementia. Dementia is neither clinical nor pathological global diffuse process. Thus, morphological substratum varies from different diagnosis and in that context, the definition of dementia as a condition of obtained and permanently progressive mental disorder that attacks several important domains of cognitive functions, is clinical and pragmatic. Characteristics of typical clinic presentation of dementia are multiple cognitive disorders, first of all the memory disorder, in early stage the episodic memory, with one or more disorders in verbal functions, executive functions, gnosis or practice. It is for sure that, beside mentioned patho-morphological changes of cognitive (dys)functions, the analysis of bio-chemical and genetic basis is important in gradation system of neuro-psychological changes by Alzheimer dementia. Changes of cognitive functions could be divided into early, middle and late manifestations of cognitive degradation by dementia. That could, maybe, more clearly define cognitive ageing from early symptoms of dementia, and clinical identification and clear definition would have immediate impact on therapy and planning of a progress of a disease.

Key words: dementia, Alzheimer dementia, cognitive changes, morphological substratum

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CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-05)

ASSESSMENT OF BETA STIFFNESS INDEX IN PATIENTS WITH MEMORY PROBLEMS: A PILOT STUDY

JURAŠIĆ MJ[1], Martinić Popović I[1], Liščić R[2], Demarin V[1]

[1] *"Sestre Milosrdnice" University Hospital, University Department of Neurology, Zagreb, Croatia*
[2] *Institute for Medical Research and Occupational Health, Zagreb, Croatia*
mkesic@inet.hr

Background and purpose: Recent studies have indicated that vascular risk factors are involved in the pathogenesis of cognitive disorders and dementia. Both VaD and AD, being the most common subtypes of dementia, are associated with cerebrovascular disease and different vascular risk factors. An increased pulse pressure has been associated with the prevalence and severity of cerebral white matter lesions while aortic stiffness was shown to be an independent predictor of stroke in patients with hypertension. Lesions of cerebral microvessels due to cerebral amyloid angiopathy, hyalinosis or microvascular degeneration induce chronic hypoperfusion of the white matter contributing to early expression of the cognitive decline. Measurement of changes of arterial beta stiffness index and circumferential arterial strain (CAS) on carotid arteries as a cerebrovascular model could be used as a screening method for the structural and functional changes of the cerebrovascular tree in patients with memory problems.

Methods: We studied the association between cognitive function and arterial beta stiffness index in 40 elderly subjects reporting memory problems. Neuropsychological evaluation was performed using MMSE, CDR (Clinical Dementia Rating) and MoCA (Montreal cognitive assessment). Subjects were categorised into three groups according to neuropsychological evaluation: mild cognitively impaired patients (MCI; CDR => 0,5; n=12), Alzheimer disease (AD; n= 16) and vascular dementia (VaD; n=12). Control group consisting of 30 subjects with no subjective or objective memory problems was used for comparison. Carotid arteries were used as a cerebrovascular model in both groups and beta stiffness index as well as CAS were measured, using Aloka SV-5500 with linear probe 5MHz for e-tracing and 13 MHz for morphologic evaluation.

Results: After adjustment for age, gender, education level and modifiable vascular risk factors, we observed a significant association between cognitive status and both arterial beta stiffness index and CAS ($p<0,005$).

Conclusions: Arterial beta stiffness index showed positive association with cognitive impairment in patients group, independently of major modifiable vascular risk factors. This method could be used as a non-invasive vascular screening method in patients with memory problems.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-03)

TAKING CARE OF THE PATIENTS WITH ALZHEIMER'S DISEASE IN THE PSYCHIATRIC HOSPITAL UGLJAN

LABURA D

Psychiatric Hospital Ugljan, Ugljan, Croatia
zd.labura.d@inet.hr

The Psychiatric Hospital Ugljan has in its hospital structure the Ward for the Social Care of the aged persons with psychic health problems, recently opened (September, 2004). The capacity of this Ward is twenty beds. By the Permission of the Ministry (The Department of Health and Social Security) this ward gives full board accomodation, care, nursing, stay, treatment and rehabilitation of the persons, mostly with the diagnosis of dementia, caused by different reasons. The patients with Alzheimer's disease prevail. Ward patients enter into an agreement directly with

the Institution (Contract form) for the accomodation (15 EURO per day) or they do it through the Centre for Social Security and then the accommodation price is bigger (18 EURO p. d.).They are accommodated in specially arranged rooms, ten of them, so there are only two patients in every room. Rooms are premises are air-conditioned and specially technically equipped for the accommodation of such specific patients (specialized beds, with moveble headboards, with possibility of feeding in the bad, and also with special parts for the treatment of injuries of the extremities). There are the video-cameras for monitoring in some rooms and they are for the patients who are in the acute phase of treatment beacuse of the specific somatic disease or their condition demands the constant monitoring. The staff is equipped in a way to provide the best possible care for the nursing patients. In one shift, there are two nurses, two professional helath care givers and the female assistant in the ward kitchen. During the morning shift the responsible person for the ward is the matron, with higher degree of education (qualification). Every day there is medical visit -rounds for the patients, done by the room physician, and during the duty the psychiatric monitoring. There is also the possibility for the regular blood and biochemical parameters controls in the laboratory, internal medicine specialist examination, EEG and X-ray screening. The ward patients can also be visited by the occupational therapist who helps them to organize their free time in the occupational treatment or they can spend their time in the ward living-room, watching TV or communicating with their health assistants or mutually.

The care for the patients enables them to feel like they are in their own homes, surrounded by the kindness and appropriate attitude. Nice Mediterranean climate and vegetation, beautiful park where the patients can

walk around, all the contributes to the therapeutic effect. These conditions slow down the dementia states and especially in patients with Alzheimer's disease. The change of the environment and the accommodation in our facilities havent had the negative effect on the disease, but on the contrary.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-06)

EARLY ASSESSMENT OF MILD COGNITIVE DECLINE IN PATIENTS WITH CEREBROVASCULAR DISEASE

MARTINIĆ POPOVIĆ I[1], Šerić V[1], Jurašić MJ[1], Liščić R[2], Demarin V[1]

[1] "*Sestre milosrdnice*" *University Hospital, University Department of Neurology, Zagreb, Croatia*
[2] *Institute for Medical Research and Occupational Health, Zagreb, Croatia*
irene@post.htnet.hr

Background and purpose: Discrete signs of cognitive decline are known to exist in preclinical dementia of both Alzheimer's or vascular type. The importance of cerebrovascular risk (CVR) factors in the pathogenesis of dementia of both types is stressed by the results of recent studies.

Methods: Patients (PGs) with first ever stroke or TIA (N=110) and asymptomatic subjects-controls (CGs) with cerebrovascular risk factors (N=45) were tested using Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) on addmition, at three- and six-months points.

Results: In all subjects initial MMSE was normal, while in 52 PGs and 11 CGs initial MoCA score was decreased (‹26 points). Cognitive performance on MMSE for both groups throughout the study period fell within the normal range, while MoCA scores revealed cognitive abnormalities: after three months in PGs, and after six months in PGs and CGs. Intra-group differences in cognitive decline (ΔMoCA) were statistically significant for PGs with stroke/multiple risk factors and PGs with TIA, PGs with stroke and PGs with TIA. There was no significant difference in ΔMMSE for PGs with stroke and PGs with TIA and ΔMoCA in PGs with TIA and ΔMoCA in CGs (p=0,053).

Conclusions: MoCA enables early detection of mild cognitive changes in symptomatic patients with cerebrovascular disease, but also in asymptomatic individuals with increased cerebrovascular risk in whom strong medical control of modifiable vascular factors may prevent occurence of severe dementia.

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PHARMACOTHERAPY OF DEMENTIA

MIHALJEVIĆ-PELEŠ A[1], Kudlek-Mikulić S[1], Šagud M[2], Živković M[3], Jakovljević M[4]

[1] *Clinical Hospital Center Zagreb, Department of Psychiatry, Zagreb, Croatia*
[2] *"Dr Ivan Barbot" Neuropsychiatric Hospital, Popovača, Croatia*
apeles@mef.hr

Pharmacological treatment of dementia is real challenge in every day psychiatric praxis. Especially it is a problem in patients with agitation, aggression and psychotic symptoms. Despite usage of many drugs, there is no real recommendation for the treatment of demented patients. Near by recommended drugs for cognitive function, for the control of agitation, aggression and psychotic symptoms antipsychotics are very often in the usage. However, new antipsycotics are not recommended due to risk of cerebrovaskular incidents. Therefore old antipsychotics are still dominant in the therapy, despite unacceptable adverse events profile.

In this article we analysed pharmacological treatment of dementia in 54 hospitalised patients in the Department for psychiatry KBC during 2005. The most often was used sulpiride. Other antipsychotics have also been in the usage.

At the and we can conclude, that there is no algorithm for the pharmacological treatment of dementia. Classic antipsychotics are still dominant in the therapy of demented patients, despite their unacceptable adverse events profile. Due to good adverse events profile of new antipychotics, they could be better choice for the treatment of agitation, aggression and psychotic symptoms. In the view of the risk for cerebrovascular adverse events, new antipsychotics, should be targeted towards the treatment of those patients in whom behavioural and psychotic symptoms of dementia are associated with significant distress, functional impairment or danger to the patient.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-08)

NEUROPSYCHOLOGICAL EVALUATION OF COGNITIVE DISORDERS AND PERSONALITY CHANGES IN PATIENTS WITH ALZHEIMER DISEASE

PAČIĆ-TURK LJ

Clinical Hospital Center Zagreb, Department of Neurosurgery, Medical School University of Zagreb, Zagreb, Croatia
ljiljana.pacic-turk@zg.t-com.hr

Having in mind that the world population is growing older, we have to emphasize the increased need for medical and psychological care of older people. The major role of neuropsychological assessment is to determine whether a patient is experiencing cognitive and executive functions deficits and personality changes due to his normal aging process or starting process of dementia.

Dementia is a clinical syndrome characterized by deficits of cognitive functions which impair the patient's social and occupational functioning. Moderate to severe dementia occurs in 2% of persons between the ages of 65 and 69 and 16% above the age of 79.

Alzheimer disease is the most common dementing disorder in older individuals, and the neuropsychological assessment plays a critical role in the early diagnosis of AD. The neuropsychological symptoms at the early stage of illness include dysfunction in recent memory and attention and executive functions deficits together with impaired naming, ending with complete unawareness of severe deficits including aphasia, apraxia, agnosia and disorientation.

Subtypes of AD usually include predominantly verbal, visuospatial or global deficits. The other classification distinguishes between early-onset AD (before the age of 65, having more rapid deterioration and more severe deficits of attention and executive functions) and late-onset disease.

Some studies report the relatively high prevalence of apathy and depression among AD patients, more likely in patients with mild to moderate cognitive impairment.

Neuropsychological evaluation can be very useful in determining the etiology of dementia, and four types of dementia can be distinguished: Alzheimer and frontotemporal dementia (early symptoms including personality and mood disorders, executive functions deficits, perseverations), cerebrovascular and Lewy bodies dementia (early symptoms including verbal fluency, executive and visuospatial deficits and hallucinations), Parkinson and other subcortical dementias and dementias as a consequence of craniocerebral injuries, metabolic changes etc.

It must be emphasized that, for the treatment of deficits, it is very important to distinguish between dementia and pseudodementia in depression.

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SPEECH-LANGUAGE DIFFICULTY IN ALZHEIMER'S DISEASE PATIENTS

PRIZL JAKOVAC T

Faculty for Education and Rehabilitation, Zagreb, Croatia
tatjana.prizl-jakovac@vz.htnet.hr

Background: The most common cause of irreversibile dementia is Alzheimer's disease. Individuals with early Alzheimer's disease consistently perform poorly on test of episodic memory, such as verbal recall tasks, working memory, deficits in verbal and visuospatial tasks, and semantics memory sush as naming, category knowledge, attribute knowledge and verbal fluency. The aim of this study was to examine and compare speech-language functioning on persons with aphasia and persons with dementia.

Method: The survey comprised 6 subjects (3 aphasics, 3 AD patients) of both genders, aged between 54 and 60. In this study Everyday Life Activities, Object Photo Series (Stark, 2003.) manual was used with which we tried to provide insight in characteristics of speech-language functioning in above mentioned groups. We also wanted to see if there are any differences between them. Study material consists of four groups of tasks. Two of them are verbal and the other two are non-verbal. Verbal tasks examine comprehension and usage of prepositions and vocabulary, whereas non-verbal tasks examine the memory abilities and structure of words. Qualitative Analysis of Errors was made because of small number of examinees. All results are presented numerically and in percentages.

Results: According to our expectations AD Patients showed significantly worse results on all applied tasks than aphasia patients. Subjects with aphasia had most difficulties in tasks which were more linguistically demanding, while the subjects with dementia had difficulties also in cognitive task that examined memorizing. The group of exeminees with Alzheimer dementia achieved 16 points (22%), while the group of exeminees with aphasia achieved 50 points (70%).

Conclusion: Considering speech-language and cognitive difficulties noticed at people with dementias, the achieved results are in concordance with various literature quotations. Memory loss is the hallmark symptom of Alzheimer's disease. Although, there is a gradually worsening of semantic abilities, including increased word -finding deficits, increased use of indefinite pronouns and difficulty comprehending complex instructions. Short-term memory losses are reflacted in increased forgetting a topic conversation and receptive verbalization. All AD patients showed outstanding language difficulties, just like examinees with aphasia.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-10)

THE ROLES OF SPEECH-LANGUAGE PATHOLOGISTS WORKING WITH INDIVIDUALS WITH DEMENTIA

PRIZL JAKOVAC T, Leko A

Faculty for Education and Rehabilitation, Zagreb, Croatia
tatjana.prizl-jakovac@vz.htnet.hr

In many world countries speech-language pathologists are members of an interdisciplinary team of professionals who diagnose and treat older people with dementia. Assessment and treatment goals are to determine the nature and extent of the language deficit, to enable the patient to maintain as much functional language as possible, given the course of the dementing disease, and to monitor the patient's language capabilities for progressive involvement.

In Croatia, dementia patients do not have methodically organized care and appropriate services that would benefit the individual and maximize cognitive-communication functioning at all stages of the disease process. More or less we do not have any speech language pathologists who play a primary role in the screening, assessment, diagnosis, treatment and research of cognitive-communication disorders, including those associated with Alzheimer's disease.

Most of the current treatment strategies for cognitive-language disorders common to dementia originated from clinical aphasia treatment models. The efficacy of aphasia therapy has been explored in numerous and varied researches. Although treatments for aphasic disorders have proved to be efficacious in general, they may not be appropriate for treating the more global cognitive-language disorders in dementia. Treatment approaches have been developed to address the specific problems of dissolution of memory, reality, emotions and semantic content. The Arizona Battery for Communication Disorders of Dementia (ABCD, Bayles and Tomoeda, 1991) is the most commonly used assessment available for evaluating dementia and language deficits.

Dementia patients need structure and routine for optimal performance. Stimulus materials should have saliency for the patient's daily living environment. Functional therapy enhances patient's ability to relate an object with daily activities within the home environment. Dementia patients communicate best in a face-to face client-patient encounter in a quiet, orderly environment.

Patients with dementia should be diagnosed with a variety of instruments for cognitive and language status. The goals for evaluation are to assess cognitive-language disorders, determine functional status, predict outcome, and monitor functional change. Rehabilitation strategies should be designed to enable the patient to remain independent as long as possible.

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CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-11)

PROGRESSION OF ALZHEIMER'S DISEASE AFTER ONE YEAR

SISEK-ŠPREM M, Folnegović-Šmalc V, Makarić G

University Department of Psychiatry, Psychiatric Hospital Vrapče, Zagreb, Croatia
mirna.sisek-sprem@bolnica-vrapce.hr

Aim: The purpose of the study is to show intensity of progression of Alzheimer' disease viewed through their cognitiv and functional capabilities and their change of behavior, during the period of one year.

Methods: Research included 30 patient which were treated at the hospital Vrapče during 2002. and 2003. with the possible diagnosis of Alzheimer' disease (ICD X criteria). The degree of cognitive decline (that corelates with the stage of the illnes) was measured by using MMSE (Mini Mental State Exam) scale. For measuring functional abilities we used MOSES (Multidimensional Observation Scale for Eldery Subjects) scale, and for measuring behavioural disturbances of Alzheimer's patients we used NPI (The Neuropsychiatric Inventory) scale.

Results: Average cognitive capabilities (MMSE):

- in first measuring was 15,50 points
- in second measuring it was 10,76 points

After one year cognitive decline was 4,734 points.

Functional capabilities (MOSES):

- in first measuring was 83,2 points
- in second measuring it was 109.3 points

Higher result in MOSES scale represent less of functional capabilities.

Behavioural disturbances (NPI):

- in first measuring was 33,5 points
- in second measuring it was 51,05

Higher result in NPI scale means that number and intensity of simptoms are higher.

Conclusion:

1. Average cognitive decline was 4,734 points (16 %) after one year time.
2. After a year there is a significant decline in functional capabilities and behavioural disturbances in Alzheimer patients.
3. Funkctional capabilities and behavioural disturbances corelate with cognitive decline but there is even a stronger corelation between cognitive decline and functional capabilities.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-12)

EPIDEMIOLOGY OF DEMENTIA ON THE DEPARTMENT OF NEUROLOGY UNIVERSITY HOSPITAL OSIJEK

SOLDO-BUTKOVIĆ S, Hegeduš I, Tomić S, Jurić S

University Hospital Osijek, Department of Neurology, Osijek, Croatia
s.filipovic@vip.hr

Aim: In our retrospective study we have analysed patients diagnosed as dementia, cognitive deficit and patients who, apart from dementia, suffered from other primary and secondary diseases. Methods: The data were collected from medical records and case histories within the period from January 1st 2005 to January 31st 2006, i. e. within one year. According to the anamnestic data, neurological and clinical examination findings and neurological - radiological diagnostics, as well as definitions criteria for different types of dementias, we grouped the patients suffering from following dementias and compared the groups according to the number of patients in each of them: Alzheimer's disease (AD), mild cognitive impairment (MCI), vascular dementias (VD) and other dementias as consequence of some other neurological and non-neurological diseases (multiple sclerosis, Parkinson's disease, brain tumor, alcoholism).

Results: Out of 1842 patients suffering from different neurological diseases, who were hospitalized in the examined period, there were altogether 139 patients suffering from all types of dementia (7,5 %). We excluded the patients with psychiatric diseases and diagnoses which could be falsely disguised as dementias. Out of those 139 patients, according to diagnostic criteria the following percentage of different types of dementias has been displayed: 84 vascular dementias (60%), 26 Alzheimer's disease (19%), 10 MCI (7%), and 19 other dementia sindroms (14%).

Conclusion: Our results indicate the greatest incidence of vascular dementias. In the literature, Alzheimer dementias represent the greatest incidence. Reason for this incosistency from world data is in fact that most of the demented patients we treated as out-patients. Also, some of the patients diagnosed as vascular dementia maybe had comorbidity of Alzheimer dementia with stroke that become evident just after the stroke and are misdiagnosed, that can only be confirmed with the patohistological findings.

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CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-13)

DELIRIUM EPISODE AS SIGN OF UNDETECTED DEMENTIA

SVRDLIN P, Šain I, Devčić S, Grošić V, Mihanović M

"Sveti Ivan" Psychiatric Hospital Zagreb, Croatia
perosvrdlin@yahoo.com

Dementia is characterized by decline an intellectual functioning to the extent that the patient is unable to perform the usual activities of daily living. Memory deficit is a predominant component of dementia, and the deterioration may occur over months to years.In elderly persons, dementia is the most common risk factor for delirium.

A delirium episode is often the first sign of dementia requiring attention from medical and social professionals.Delirious patient with dementia tended to have more symptoms of delirium than delirious patient without dementia. Delirium is an important prognostic marker for functional and cognitive status for at least 12 months after admission among patients with dementia. Delirium in patients with dementia increases the likelihood of transfer to a long-term care institution.

This case is about patient N.D. aged 78, who was admitted to our hospital and was diagnosed delirium.He was not diagnosed dementia before delirium appeared.A year before the appearance of delirium his activities and social interactions gradually started to reduce. Dementia was predisposing factor for delirium, while urinary tract infections was its precipitating factor which was also the reason for his hospitalization in general hospital for the first time.

After curing his urinary tract infections he was transfered to our hospital in the state of delirium.When his delirium was lessened, his intellectual functioning was deteriorated to such extent that he was not able to perform his daily activities so he had to be transfered to a long term care institution.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-14)

DELIRIOUS STATE PRODUCED BY VASCULAR DEMENTIA ASSOCIATED WITH RHEUMATIC VALVULAR HEART ABNORMALITIES WITH VARIETY OF OTHER CARDIAC DISEASES

ŠENDULA-JENGIĆ V, Ružić T, Katić P, Višić V

Rab Psychiatric Hospital, Rab, Croatia
psihijatrija-rab@ri.htnet.hr

This is a case report of 67-years old man with a prior history of rheumatic fever and one episode of acute pulmonary edema. During the hospital treatment on Neurological clinic, of complex progressive neurological deficiencies, the patient developed dellirant confusion state during which he assaulted and killed another patient. Using computerized tomography, the diffuse ischemic brain disease with multiple lesions and significant cerebral atrophy were found. Cardiology examination had shown severe mitral stenosis with paroxysmal atrial flutter and preserved systolic left ventricle function.

We illustrate the case of apparently unconnected clinical manifestations from acute heart failure to acute psychotic episode with crime consequences, in clinical picture of vascular dementia.

Key words: delirious state, vascular dementia, valvular heart abnormalities.

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HAS CHOLESTEROL A ROLE IN PATHOGENESIS OF DEMENTIA?

TRKANJEC Z, Bašić-Kes V, Martinić Popović I, Jurašić MJ, Demarin V

"*Sestre milosrdnice*" *University Hospital, Department of Neurology, Zagreb, Croatia*
ztrkanj@kbsm.hr

Dementia is a significant cause of morbidity and mortality in elderly people. Recent studies have shown the vascular dementia and Alzheimer's dementia might overlap in many aspects. Also it was suggested that elevated cholesterol could have some influence on Alzheimer's dementia onset and progression.

The aim of study was to evaluate the levels of cholesterol in patients with Alzheimer's dementia (AD) and vascular dementia (VaD).

Sixty-six patients with dementia were enrolled in this study. AD was diagnosed in 43 and VD in 23 patients.

In a group of 43 patients (22 males and 21 females) with AD, mean age 72,79 years (standard deviation /SD/=8,19 years), and in a group of 23 patients with VaD, mean age 77,43 (SD=7,58) plasma values of cholesterol were analyzed.

In AD group 18 patients had normal, and 25 had elevated plasma cholesterol levels, while in VaD group 12 patients had elevated and 11 had normal plasma cholesterol levels. Mean plasma level of total cholesterol was 5,39 (SD=1,05), LDL cholesterol was 3,33 (SD= 0,95), and HDL cholesterol was 1,41 (SD= 0,34) in patients with AD. In patients with VaD mean plasma level of total cholesterol was 5,78 (SD=1,06), LDL cholesterol was 1,44 (SD=0,57), LDL cholesterol was 3,72 (SD=0,85).

The levels of cholesterol, LDL cholesterol, HDL cholesterol were higher in group of patients with VaD, but the difference did not receive statistical significance.

It is well known that VaD is associated with vascular risk factors. However, our data show that patients with AD also have elevated plasma levels of cholesterol. Results of this study support the idea that cholesterol could have some influence on etiology, onset and progression of AD, as well as on pathogenesis of VaD.

CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-16)

POTENTIAL INFLUENCE OF HYPERTENSION ON PROGRESSION OF DEMENTIA

TRKANJEC Z, Morović S, Demarin V

"*Sestre milosrdnice*" *University Hospital, Department of Neurology, Zagreb, Croatia*
ztrkanj@kbsm.hr

Dementia is a growing problem of modern society causing significant percentage of morbidity and mortality in elderly people. Two major causes of dementia are vascular diseases and Alzheimer's disease. Recently it has been suggested that vascular dementia and Alzheimer's dementia might overlap in many aspects. Also it was suggested that vascular risk factors could have a role in Alzheimer's dementia onset and progression.

Hypertension is one of the most significant risk factors for vascular diseases.

The aim of study was to evaluate the role of hypertension in patients with Alzheimer's dementia (AD) and vascular dementia (VaD).

Sixty-six patients with dementia were enrolled in this study. AD was diagnosed in 43 and VD in 23 patients.

Hypertension was diagnosed if a patient had values higher than 130/85 on two successive measurements during different days, or if a patient was taking antihypertensive medication.

In a group of 43 AD there was 24 patients with hypertension, and 19 patients were normotensive. In a group of 23 VaD patients there were 16 patients with hypertension and 7 patients were normotensive.

Higher proportion of VaD patients had hypertension compared with AD group. However, hypertension was also present in significant proportion of AD patients.

It is well known that VaD is associated with hypertension as on of the most prominent vascular risk factors. Data from this study show that in patients with AD there is also significant proportion of hypertension, supporting the idea that hypertension could also have some role in etiology, onset and progression of AD, as it has on pathogenesis of VaD.

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CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-17)

TREATMENT OF AGITATED PATIENTS WITH ALZHEIMER'S DEMENTIA

UZUN S[1], Kozumplik O[1], Mimica N[1,2], Folnegović-Šmalc V[1,2]

[1] *University Department of Psychiatry, Psychiatric Hospital Vrapče, Zagreb, Croatia*
[2] *School of Medicine, University of Zagreb, Zagreb, Croatia*
suzana.uzun@bolnica-vrapce.hr

Objectives: to compare changes in symptoms of agitation in the groups of patients with Alzheimer's dementia treated with typical and atypical antipsychotics, measured by Agitated Behavior Scale.

Methods: Agitated Behavior Scale was used in order to assess symptomatic improvement in two groups of agitated patients with Alzheimer dementia. Each group was comprised of 15 patients (8 male 7 female (typical antipsychotics); 7 male, 8 female (atypical antipsychotics)). Patients were assessed during period of 1 month of continuous treatment with antipsychotics. All patients were inpatients. In the group treated with typical antipsychotics 10 patients were treated with haloperidol (2-6 mg) and 5 patients with flufenazine (2,5-7,5 mg). In the group treated with atypical antipsychotics 6 patients were treated with quetiapine (100-300 mg), 5 patients were treated with olanzapine (5-10 mg) and 4 patients with risperidone (2-4 mg).

Patients began therapy with antipsychotics after being admitted on our Clinical department. The first assessment (baseline) was made upon the inclusion. In the first 5 days, assessments were performed on the daily basis. After that, patients were assessed every week. Beside antipsychotics, patients were treated with hypnotics.

There were 3 cases of therapy discontinuation due to side effects (extrapyramidal symptoms, hypotension, weight gain). The patients who discontinued the therapy were assessed on the last day of therapy, and their results were added to the results of other patients.

Results: Improvements in symptoms occurred during first 5 days of treatment in both groups, measured by Agitated Behavior Scale (total score). During this period, in the group treated with atypical antipsychotics improvements occurred regarding impulsive, impatient, low tolerance for pain or frustration, violent and/or threatening violence toward people or property, explosive and/or unpredictable anger, restlessness and pacing. During the same period, in the group treated with typical antipsychotics improvements occurred regarding impulsive, impatient, low tolerance for pain or frustration, violent and/or threatening violence toward people or property. After one month of therapy, clinically significant improvement was present in the group

treated with atypical antipsychotics regarding impulsive, impatient, low tolerance for pain or frustration, violent and/or threatening violence toward people or property, explosive and/or unpredictable anger, restlessness and pacing, rocking, rubbing, moaning or other self-stimulating behavior. In the same period of time in the group treated with typical antipsychotics improvements have occurred regarding impulsive, impatient, low tolerance for pain or frustration, violent and/or threatening violence toward people or property, explosive and/or unpredictable anger.

Conclusion: the presented study was performed before Food and drug administration (FDA) came up with the warning regarding use of atypical antipsychotics in elderly patients. No side effects mentioned in the FDA's warning emerged during our study. Both treatments with typical and atypical antipsychotics have proved to be good choice in agitated patients with Alzheimer dementia. Treatment with atypical antipsychotics was more successful according to the Agitated Behavior Scale.

References:

1. Uzun S, Kozumplik O, Mimica N, Folnegović-Šmalc V. Nuspojave psihofarmaka. Zagreb: Medicinska naklada, Psihijatrijska bolnica Vrapče; 2005.
2. Kozumplik O, Uzun S, Folnegović-Šmalc V, Jukić V, Mimica N. Clinical diagnosis of Alzheimer's disease: Importance of rating instruments. Neurologia Croatica, Book of abstracts, The First Croatian Congress of Neuroscience, November 21-22, 2003, Zagreb.
3. Bogner, J., Corrigan, J.D., Stange, M., & Rabold, D. Reliability of the Agitated Behavior Scale. Journal of Head Trauma Rehabilitation 1999;14:91-96.

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CONTEMPORARY CLINICAL APPROACH TO ALZHEIMER'S DISEASE (PP-C-18)

PHARMACOTHERAPY OF DELUSIONS IN ALZHEIMER'S DISEASE

VIDAS-KAĆANSKI A, Višić V

Rab Psychiatric Hospital, Rab, Croatia
marko.barcic@ri.t-com.hr

This is a case report of 82-years old female patient with Alzheimer disease with predominant psychotic expression. During treatment of psychotic expression of disease patient has been treated with various types, dosage and combination of antipsychotics. On all kinds of antipsychotics she has developed severe side effects of treatment. Because of insufficient remission, complex and progressive clinical picture, as well as because of pharmacotherapeutic resistance, during hospitalization implementation with olanzapin has bean proceeded. With olanzapin we have succeeded to reduce psychopathological elements with consequentially slowing down progression of disease. Even if during treatment with olanzapin memory and cognitive dysfunction has not bean healed, because of reducing of symptoms, physiological and social functions has bean preserved during longer period of time.

We illustrate efficiency of olanzapin in treatment of Alzheimer disease, on patient with psychotic elements with presence of therapeutic resistance on other antipsychotics.

Key words: Alzheimer's disease, delusions, olanzapin.

POSTER PRESENTATIONS

CURRENT TRENDS IN ORGANIZATION OF SELF-HELP GROUPS AND CARE-GIVERS EDUCATION

PP-G-(01-08)

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CURRENT TRENDS IN ORGANIZATION OF SELF-HELP GROUPS AND CARE-GIVERS EDUCATION (PP-G-01)

TEN EARLY COGNITIVE AND BEHAVIORAL DEFICITS IN ALZHEIMER'S DISEASE

BOBAN M[1], Boban Ma[2], Mladinov M[1], Radoš M[1], Grbić K[1], Dejanović N[1], Mimica N[3], Šimić G[1]

[1] *Croatian Institute for Brain Research, Zagreb, Croatia*
[2] *Clinical Hospital Center Zagreb, Department of Neurology, Medical School University of Zagreb, Zagreb, Croatia*
[3] *Psychiatric Hospital Vrapče, University Department for Psychiatry, Zagreb, Croatia*
marcoboban@yahoo.com

Alzheimer's disease is the most common cause of dementia, with global increase of 4.6 millions cases each year (whole Croatia). Main characteristic of disease is substantial cognitive impairment with domination in memory loss. In this poster we presented commonest cognitive and behavioral landmarks suggesting pre-clinical Alzheimer's disease. Those ten symptoms and signs are presented in a way to be detected even by untrained individual and were proposed by Alzheimer's disease International (ADI).

CURRENT TRENDS IN ORGANIZATION OF SELF-HELP GROUPS AND CARE-GIVERS EDUCATION (PP-G-02)

ALZHEIMER'S DISEASE - DIAGNOSTICS AND THERAPY - CONDITION IN VUKOVARSKO SRIJEMSKA COUNTY

DEJANOVIĆ N, Dejanović V

General Practice in Nuštar, Nuštar, Croatia
dejanovic@yahoo.com

Background: According to information from literature every tenth person over the age of 65 has a form of dementia and according to epidemiological estimates there are about 50000 demented people of senior age in Croatia, out of which over 30000 have Alzheimer's disease. Accurate data are not known.

Aims: of this research/survey is to find out the real condition of diagnostics and therapy of Alzheimer's disease in total population of people over 65 in Vukovarsko Srijemska County and to compare the results with the estimates and expectations from the literature. The main proposition is that Alzheimer's dementia is underdiagnosed.

The results could be guidelines in improvement of diagnostics and therapy of AD in Croatia.

Methods: Based on data of total number of health insured in the County (N = 174297) and on data of registered older than 65 (N = 31999) in general practice (N = 90), with the inspection of medical documentation, the information on three searched variables of each surgery have been gained:

- the number of registered in general practice with suspected dementia,
- the number of patients with diagnosed Alzheimer's disease and
- frequency of prescribing drugs for dementia available according Croatian Drug Register 49/2006 (donepezil and memantin).

Results: Results show that in general practice Vukovarsko Srijemska County, where the total number of registered per practice/team ranges from 1000 to 2200, there are mostly from 200 to 560 patients over the age of 65. Out of that number, there are from 0 to 15 with suspected dementia and there is most frequently none or one patient with diagnosed Alzheimer's dementia.

The frequency of prescribing drugs for dementia (registered drugs: donepezil and memantin) is negligibly small, almost zero.

Comparing to epidemiological estimates, according to which there are 2 to 10% patients with Alzheimer's disease in people over the age of 65 in Croatia, results in the population of one County show that this percentage is less than 1.

Conclusion: The dissimilarity in results (much less number of diagnosed AD in comparison to epidemiological estimates), can be interpreted in different ways: there really aren't so many cases of AD in examined population as it is expected from the estimates; the population sample is not typical for the whole Croatia in number and/or structure; or results show that AD is underdiagnosed (too small number of diagnosed cases in relation to the real situation). The explanation of underdiagnosed cases seems possible because of: the disease is not recognized by the patient's close family, low socioeconomic status and/or the family attitude to dementia, the lack of reliable diagnostic guidelines, the lack of equipment and experts, excessive load of curative and acute diseases, the lack of education and informing of patients and doctors of the necessity and efficiency of treatment of AD and the improving of the quality of life.

CURRENT TRENDS IN ORGANIZATION OF SELF-HELP GROUPS AND CARE-GIVERS EDUCATION (PP-G-03)

1906 - 2006: 100 YEARS OF ALZHEIMER'S DISEASE

IVANKOVIĆ V[1], Grbić K[2], Šimić G[2], Mimica N[3]

[1] *Alzheimer Disease Societies Croatia, Zagreb, Croatia*
[2] *Croatian Institute for Brain Research, Zagreb, Croatia*
[3] *Psychiatric Hospital Vrapče, University Department of Psychiatry, Zagreb, Croatia*
alzheimer@alzheimer.hr

Although the disease was named one hundred years ago, it exists from the ancient times. First ones to describe it were old Grecian and Roman writers, later Shakespeare and other medieval authors. The disease term was varying throughout the different cultures and times. Its name, the disease owes to Alois Alzheimer, German scientist, who described it in 1906 on the 51 year-old patient Augusta D.

Despite the enormous effort and great amount of data, one hundred years after the description, we still don't understand the exact cause and changes within the disease. Therefore Alzheimer's disease accurately holds the epithet "enigma of all enigmas".

In 1984, Alzheimer Disease International (ADI) was founded as a head world's organization for Alzheimer's disease. Croatian association for Alzheimer's disease was founded in 1999 and became a member of ADI in 2005. From 1994 ADI, with the support of World health organization (WHO), annotates World Alzheimer's Day. World Alzheimer's Day™, 21 September each year, is a day on which Alzheimer associations concentrate their efforts on raising awareness about dementia. There are an estimated 24 million people around the world who currently have dementia including more than 50 000 in Croatia.

Getting people to campaign collectively on a unifying theme in their country is the most effective way of bringing dementia to the global attention of governments, opinion leaders, medical professionals, people with dementia and their care-givers. The importance of education is also outlined, not only for experts, but patients and their families. As this year's ADI motto says there is no time to lose!

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CURRENT TRENDS IN ORGANIZATION OF SELF-HELP GROUPS AND CARE-GIVERS EDUCATION (PP-G-04)

ALZHEIMER'S DISEASE IN ZAGREBS HOSPITALS

LEPPÉE M[1], Štimac D[1], Koščak D[2], Polić-Vižintin M[1], Čulig J[1]

[1] *Zagreb Public Health Institute, Zagreb, Croatia*
[2] *Bjelovar General Hospital, Bjelovar, Croatia*
marcel.leppee@publichealth-zagreb.hr

Aim: The aim of the paper is to present and analyze the rate of Alzheimer's disease in Zagreb hospitals, and to point to the extent of this public health problem.

Methods: Data on the patients with Alzheimer's disease treated at Zagreb hospitals from 2000 till 2005 were included in the study. Data were obtained from the database of inpatient records, referring to particular persons and entered in respective forms for each individual hospitalized patient. The main diagnoses are described by the codes provided by ICD-X, the given diagnosis being G30 including F00*.

Results: About 250 patients with Alzheimer's diseases, with 9000 to 10000 hospital days, were treated at Zagreb hospitals per year. The average duration of treatment was 45,6 days. Alzheimer's disease was more common in the >70 age group, who accounted for 70% of all Alzheimer patients, and women accounted for 65% to 70% of Alzheimer patients, which could be ascribed to the higher life expectancy in women.

Conclusion: The aging trend observed in the general population is expected to result in an ever increasing incidence of Alzheimer's disease, thus requiring an interdisciplinary approach in the treatment of this disorder. The societies of Alzheimer patients and day-care facilities play an important role in the management of the disease, offering the patients medical care, helping them in daily activities, and assisting them in the process of socialization.

CURRENT TRENDS IN ORGANIZATION OF SELF-HELP GROUPS AND CARE-GIVERS EDUCATION (PP-G-05)

TO ASSURE SAFE RESIDENCE FOR PEOPLE WHO ARE SUFFERING FROM ALZHEIMER'S DISEASE

LESKOVIČ LJ

Nursing Home "Center", Ljubljana, Slovenia
lili.leskovic@siol.net

If we look into the future we will see that the number of elderly will increase and likewise the number of people with Alzheimers disease will increase in our residence. Such population arguments foresight dictates that we must arrange rooms for people with Alzheimers disease in existing social institutions while considering personal needs.

At an old (mature) age disease changes, among an individual, often express themselves in chronic or progressive shapes. A typical form of progressive old age disease is a brain change such as dementia (can be linked/associated to/with Alzheimer disease). "Even if dementia can occur in the middle age, majority of people are affected later in life (Pečjak, 1998: 144). In 1986 there was a study in G. Britain, Australia, New Zealand , Denmark, Sweden and Japan that showed that the percent of affected people rises with age (Preston, 1986 in Pečjak, 1998).

Dementia means (bad) decline in reasoning/intellect functions. Symptoms associated with dementia are: distinctive memory impairment, ineffective mentality, confused speech, loss of orientation in space and time, un understanding of social interactions and un ability to perform one's vocation and personality changes. Disease has a distinct progressive character and it gets worse for the patient every year.

A. Start of disease or first phase is similar to normal declination of brain functions at an old age
B. Second phase follows, where disturbances increase: confusion, great loss of attentiveness, extent of memory is reduces to only several units
C. In third phase the memory loss is so great that the patient does not even recognize his relatives.

The most frequent form of dementia is Alzheimer disease. Quick declination of neurons and gathering of waste in the cells is typical for this disease. Decay is so great that the brain shrinks considerably.

Providing security - safe "elderly home" environment

Under the expression - suitable living and home environment we understand:

A) Medical staff and health/nursing documentation:

In most cases residents with dementia are on secured sections. Providing security on secured sections is in the domain of the health care / nursing staff - or 24 hour presence of health care staff. An important part of providing security is health/nursing care documentation (ZND for future reference). For example ZND enables following of disease changes and health/nursing care needs over time (from acceptation onwards). It also makes suitable nursing plans for each individual possible. Up to date notes on each new change are possible and adjustments to health care services as well. Key significance in this context is "security of a client". Due to progressiveness of the disease - disease changes and personal needs of an individual change progressively as well which means we need to update ZND regularly. Frequent client check ups help to provide a high level of security (1). Of course here is no rule on establishing a level of security since the disease symptoms do not appear or follow in a predetermined sequence. With the level of security I wanted to warn you that the responsibility for providing security is on health care staff and that health care staff can adjust and/or change the working process - according to the disease.

B) Working with relatives:

Key factor is also an active role of the family members. For example - family are a source of information for making a ZND. Idea of "active role" means: including the family members into work process on department, cooperation at daily activities, cooperation at organization and execution of parties, picnics etc.

C) Room/space management:

- It's true that the responsibility of security is on the side of the health care staff, but without the correct space management of the secured section then health care staff is powerless. Under the idea of "room/space management" we understand:
- Arrivals and departures on secured section only under supervision; main entrance should be arranged so that allows crossing under supervision without making it look like a closed, secure section.
- Ground surface: needs to prevent potential falls (even after cleaning), they have to be from materials which are a bit rough, they need to dry fast, aren't flammable, do not contain toxic substances, do not peel off the ground.
- Wall and ceiling surfaces: need to be in nice calming colors, with limited number of electrical outlets, needs to have auxiliary framework on the walls to offer assistance while walking (at the height of hand grip), all electrical installation (wiring) should be under wall or ceiling surface.

- Tables (and other room inventory) need to have smooth round edges.
- Windows should only open on "ventus".
- Movement surfaces like living rooms or other rooms where residents reside daily need to allow free movement.
- Theme organized small nooks.
- Illuminated promenades (extra lights in dark places).

(1) Level of security: we can divide the level of security into 3 levels - low, medium, and high. Depending on the stage of the disease the requirements of security change as well. 1st stage of disease - low level of security, 2nd stage of disease - medium level of security, 3rd stage of disease - high level of security.

Institution by definition can't assure domestic environment. This is a place where you meet different people, like strangers who have to share common rooms, activities, staff, time. Because of institution order the residents have less freedom and control over their life and thus increases the degree of dependence. The perception of personal control plays a major part in feeling at home and overcoming diferent situations in collective form of living. Residents in homes have the biggest problems with accpeting new places, strangers and dependence of working staff. Specialists staff is an element of an institution, which interferes in work patterns and isn't planned or directed according to the special program, which would be helpful to relatives and not only residents, or change expected behavior of relatives and would accept relatives as individuals with individual needs in a way that would make the relatives integrated into the institution and not just as extra help to the employed staff as far as offering help to the relatives is concerned.

Slovenia built the institutional help network as a government, or as it was called - republic program after standards and unified measures of combined type of an elderly home, while Eastern European system of well fare stimulated differential institutional help, as according to its purpose (nursing homes and apartments) and ownership of the institution (private or government property).

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CURRENT TRENDS IN ORGANIZATION OF SELF-HELP GROUPS AND CARE-GIVERS EDUCATION (PP-G-06)

ACTIVITIES OF ALZHEIMER'S DISEASE SOCIETIES CROATIA

MIMICA N[1], Dajčić M[2], Ivanković V[3], Pecotić Z[4], Šimić G[5], Vidas Kaćanski A[6], Presečki P[7], Grbić K[5]

[1] *Psychiatric Hospital Vrapče, University Department of Psychiatry, Zagreb, Croatia*
[2] *Alzheimer Disease Societies Croatia, Zagreb, Croatia*
[3] *Clinical Hospital Center Zagreb, University Department of Neurology, Medical School, University of Zagreb, Zagreb, Croatia*
[4] *Psychiatry Hospital Vrapče, Psychogeriatric Department, Zagreb, Croatia*
[5] *Croatian Institute for Brain Research, Medical School, University of Zagreb, Zagreb, Croatia*
[6] *Psychiatric Hospital Rab, Rab, Croatia*
[7] *General Hospital Pula, Department of Psychiatry, Pula, Croatia*
ninoslav.mimica@bolnica-vrapce.hr

Alzheimer Disease Societies Croatia (ADSC) was founded in 1999 in Zagreb, and its branch at Rab in 2003. The main aim was to help people with dementia (PWD), their families and careers. ADSC fight stigma, brings education to target and general population. ADSC has about 550 members. We don't have paid staff, so the whole work is done by volunteers. Due to fact that Croatia has old population there is an approximation that we have today more than 50 000 people with dementia in Croatia, and belief of experts are that this number is going to quadruple by 2040. From its beginnings the ADSC has monthly meetings for families of PWD and all other interested. The ADSC has published four booklets, printed in large number and distributed in all old people homes in Croatia, send to all general practitioners, all members of ADSC and their families. Till know we have organized two Conferences on Alzheimer's disease (AD) (in Zagreb), three Symposiums on Psychogeriatrics (Rab), and numerous lectures. The members of ADSC, in many occasions, have spoken to media (TV, radio, newspapers) to raise awareness about dementia. Every year we celebrate the Alzheimer's day on September 21st. Our Society has a 24 hours help-line (**091 569 16 60**). We have our web-site (www.alzheimer.hr) and e-mail address: alzheimer@alzheimer.hr. Our work is also internationally recognized, so we become a provisional member of Alzheimer's Disease International (ADI) in 2005, and in 2006 we have applied for full membership of ADI. Two of our members attend The Alzheimer's University in London this year. In 2006 (from September 7-10) ADSC is celebrating the centenary of the identification and naming of AD, organizing 3rd Croatian Congress on Alzheimer's Disease with international participation at Brijuni, Croatia. In the near future, when we get the space, we are planning to organize the Living-room for PWD. So, for know we are lobbing for adequate office, and hope that our Government will understand our need.

CURRENT TRENDS IN ORGANIZATION OF SELF-HELP GROUPS AND CARE-GIVERS EDUCATION (PP-G-07)

ORGANISATIONAL CHALLENGES OF THE GENERAL HOSPITAL AS A PART OF THE SYSTEM NETWORK FOR TREATING DEMENTED PERSONS

PEHARDA T, Smoljanić D, Breški D

Pula General Hospital, Pula, Croatia
tomislav.peharda@pu.t-com.hr

We are witnessing an increase in the number of hospitalizations of elderly people on our wards, most of them usually with different kinds of dementia.

Patients suffering from Alzheimer's disease, marked as a specific group, seek a specific treatment, both in terms of the pharmacological therapy, as well as, considering the nature of the disease, in terms of the social care. Since there is a long-term care facility for older people and an out-patient department with a referral centre already existing in the community, there is a demand for the new form of sensibility in which a hospital would be one of the links in the integration and coordination of the network, which will then positively influence the context of hospitalisations.

We show an example of a patient in an advanced stage of dementia, who was treated for abdominal pain on several wards, but due to aggravation of her condition in the form of confusion, agitation, her staying was reduced and her treatment strictly focused. Because of the intense psychomotorical anxiety that disturbed her sleep and nourishment rhythm, the patient was finally transferred to a psychiatric ward. After she was calmed down and exposed to a thorough somatic analysis, a somatic diagnosis and a therapy were given.

This work would like to draw attention to the need for a psychogeriatric unit in the General Hospital in Pula, because of the specific conditions of elderly people and the necessity for a multidisciplinary approach, all with the view of creating one of the essential links in the network of services for older people.

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CURRENT TRENDS IN ORGANIZATION OF SELF-HELP GROUPS AND CARE-GIVERS EDUCATION (PP-G-08)

NURSING CARE IN ALZHEIMER'S DISEASE PATIENTS VIA DOCUMENTING HEALTH CARE PLAN

SUČEVIĆ V, Goljak J

Psychiatric Hospital Vrapče, Zagreb, Croatia
klinika@bolnica-vrapce.hr

The aim is formulating and presenting psychiatric nursing diagnoses in terms of Alzheimer's disease and the presentation of nursing interventions that stem from previous knowledge about the disease with the objective to assist the patient in adoption to disease.

Nursing diagnosis is a conclusion based on scientific determinates of patients health care problems, which comes out from critical analysis of his behaviour, of the disease, and numerous other factors that influence his condition.

That very conclusion is to serve as a guide in health care, while components of nursing interventions help in managing problems.

This is very important because the interventions should be adjusted to the progression of the disease and worsening of patients condition.

The interventions focused at patient's environment education are especially important.

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