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Ageing and dementia 2

EP4101

Motor neuron dysfunction in frontotemporal lobar degeneration: a clinical and neurophysiological study

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Introduction: Motor neuron disease (MND) has been reported in a proportion of frontotemporal lobar degeneration (FTLD) patients. Nevertheless, only a minority of patients develops MND at follow-up. The incidence, severity, extent and functional significance of motor neuron dysfunction (MNDys) in FTLD are still largely unexplored. In this study, we aim to evaluate the extent and distribution of clinical and neurophysiological MNDys signs in FTLD.

Methods: 71 FTLD patients were consecutively enrolled. Clinical signs of lower and upper MNDys, as well as EMG data, were recorded at baseline. Restrictive neurophysiological criteria were applied. Patients were screened for MAPT, GRN and C9orf72 mutations. Mean follow-up was two years.

Results: Overall prevalence of MNDys signs at EMG was 15.4% (i.e., 11/71 patients). Four patients (2 bvFTD and 2 PNFA; 5.6%) fulfilled El Escorial criteria for MND; the other seven showed active denervation combined to collateral reinnervation confined to either cervical or lumbar district. Moreover, at the EMG evaluation seven patients showed active denervation, and twelve isolated chronic denervation. No statistical differences in clinical phenotype, disease duration or severity were found between EMG positive and negative patients. No patient with clinical or EMG positive findings developed MND at follow-up.

Conclusion: A subgroup of FTLD patients with mild neurophysiological signs of MNDys not fulfilling criteria for MND can be found at the first diagnosis. This condition does not evolve to MND at a 2-year follow-up. Subclinical secondary degeneration of corticospinal tracts and lower motor neurons is present in the FTLD spectrum.

Disclosure: Nothing to disclose

EP4102

A 16-year network organization of memory clinics in the North of France: new patients characteristics over time

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Introduction: Memory clinics were created to improve diagnosis and management of Alzheimer’s disease. However, no data are available on the progression or their recruitment over time. We aimed at identifying changes in new patients characteristics in Northern France, where a reference memory centre runs a network of memory clinics since 1996.

Methods: We studied consecutive new consultants in all memory clinics, from 01-1997 to 12-2012, in the 4-million inhabitants Nord-Pas-de-Calais region. We collected patients’ demographic characteristics, and MMSE at entry, and who referred them. We calculated the age-, gender-, and level-of-education standardized rates of new consultants reported to the region population over time.

Results: The number of memory clinics increased from 14 in 1997 to 28 in 2012, with more geriatric settings. We observed a consistent increase of new patients (from 1565 to 6604, total=71,885) independently from the population age, sex, and level of education changes in the region, with an important increase of the oldest patients, an increased number of non-educated patients, a higher proportion of patients referred by specialists, and a shorter delay since first symptoms. The mean MMSE score remained stable around 22 except the oldest patients who consulted at a less severe stage with time. Most patients came to a close memory clinic and this proportion kept increasing except in the reference centre, where the proportion of young patients increased.

Conclusions: Our study showed that a network organization of memory clinics in a region improves access to diagnosis and care for older and less educated people.

Disclosure: Nothing to disclose
EP4103
Role of vitamin D deficiency and its receptor gene polymorphism in cognitive impairment in elderly
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Introduction: Evidences reveal that vitamin D deficiency and vitamin D receptor gene polymorphism can influence the cognitive abilities of the normal aged subjects.

Methods: The study was conducted on 50 non demented subjects ≥ 60 years old. Global assessment of cognitive function by: Modified Mini-Mental State examination test (3MS; Addenbrooke’s Cognitive Examination Revised). Assessment of specific cognitive function: For attention: Paced Auditory Serial Addition Test and Trail B test. Memory: Story A from logical memory subtest of the Wechsler Memory Scale-Revised, Paired Associate learning test and Benton Visual Retention test. Language: Token test. Visuospatial abilities: Block Design test. Measurement of 25 hydroxy vitamin D in serum and genotyping using PCR to detect the polymorphisms of VDRApaI and VDR-TaqI.

Results: Vitamin D deficiency was found to be associated with poor performance in tests assessing memory and attention, but no relation was with performance in executive functions, language or visuospatial abilities. VDR-ApaI polymorphism was found to affect memory and psychomotor speed but no effect on the performance in tests assessing attention, executive functions, language or visuospatial abilities. No effect for VDR-TaqI polymorphism on the performance in different tests.

Conclusions: Vitamin D deficiency and vitamin D receptor gene polymorphism play an important role in exacerbating cognitive impairment of normal aging.

Disclosure: Nothing to disclose

EP4104
TREM2 genetic variability in patients with Alzheimer’s disease and frontotemporal lobar degeneration
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Introduction: Mutations in triggering receptor expressed on myeloid cells gene (TREM2) have previously been associated with Nasu-Hakola disease. Recent evidence highlighted an association between rare functional variants in TREM2 and Alzheimer’s disease (AD) or Frontotemporal Lobar Degeneration (FTLD). The aim of this study has been to test TREM2 variants as susceptibility factors for FTLD and AD.

Methods: Direct sequencing has been performed in an overall Italian population consisting of 75 patients clinically diagnosed with FTLD, 607 AD patients and 612 healthy age-matched controls.

Results: Four FTLD patients (5.3%) and twelve AD patients (2%) were carriers, in heterozygosis, of different variants. In particular, one FTLD patient was a carrier of the T66M mutation, that in homozygosis state leads to Nasu Hakola disease. One FTLD patient and five AD patients were carriers of the rare variant R47H, previously associated with the development of AD. Lastly, two FTLD and two AD patients were carriers of the variant R62H, previously reported as a benign variant. Three more AD patients were carriers of Q33X mutation, that in homozygosis state leads to Nasu Hakola disease, whereas another one was carrier of the rare variant D87N. Lastly, a novel non pathological variant was found in one AD patient.

Conclusions: TREM2 could likely act as risk factor for FTLD and AD. Further studies involving a larger size population are however required to drawn definitive conclusions. Patients carrying these TREM2 variants could have a peculiar different pathogenic disease mechanism as compared with non-carriers, possibly overlapping with the Nasu-Hakola disease.

Disclosure: Nothing to disclose
**EP4105**

**Anticardiolipin antibodies are associated with cognitive dysfunction in stroke - free individuals**

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**Introduction:** The presence of anticardiolipin antibodies (aCLs) has been associated with vascular occlusive events. The role of aCLs as a risk factor for stroke has been a matter of debate, and scarce information exists on the relationship between aCLs and other cerebral disorders. Reports exist for seizures, chorea and subtle cognitive dysfunction. The association between aCLs and cognition was further explored and the relationship between aCL titres and brain magnetic resonance imaging (MRI) findings was evaluated in a large cohort of community-dwelling individuals.

**Methods:** The study cohort was drawn from the Austrian Stroke Prevention Study. A total of 1895 subjects had a complete risk factor assessment and measurement of aCL titres in serum. Participants were classified as aCL positive if either the immunoglobulin G (IgG) or IgM aCL titres were elevated (IgG>21 U/ml, IgM>12 U/ml). All subjects were also categorized based on the quartile distribution of IgG and IgM isotype titres. All underwent cognitive testing by the Mini Mental State Examination (MMSE) and a random sample of 947 participants also underwent brain MRI.

**Results:** aCL positive participants performed worse on the MMSE. IgG but not IgM isotype titres related to worse performance on the MMSE. No significant association existed with vascular brain abnormalities including lacunes, cortical infarcts and white matter lesions.

**Conclusions:** These data support the view that in normal elderly persons increasing IgG aCL titres relate to global cognitive dysfunction. It is unlikely that structural brain lesions are responsible for this finding.

**Disclosure:** Nothing to disclose

**EP4106**

**Comparison of various assessment measures on shunt effectiveness in idiopathic normal pressure hydrocephalus**

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**Introduction:** There are various measures on assessing severity of idiopathic normal pressure hydrocephalus (iNPH). The assessment may not be the same by different examiners. In the present study, we investigate the most reliable measure on shunt effectiveness between neurosurgeons and physiotherapists.

**Methods:** Forty-five probable iNPH patients were treated with ventriculoperitoneal (VP) or lumboperitoneal shunts (LP). They were assessed separately by a neurosurgeon and physiotherapists. They were included in modified Rankin scale (mRS), idiopathic normal pressure hydrocephalus grading scale (iNPHGS), functional independence measure (FIM).

**Results:** Mean age was 77 years. A VP and PL ratio was 2 to 1 and their shunt effectiveness at discharge was not different. The mRS and iNPHGS by a neurosurgeon was 51% and 78%, while those by physiotherapists were 40% and 47%. One point or more improvement on FIM by physiotherapists showed 80%. Mean value on a change of FIM total score was 8 points; 7 points on motor and 0 point on cognition. There were no statistical differences between iNPHGS by a neurosurgeon and FIM by physiotherapists on their total scores, motor scores and cognition scores.

**Conclusions:** The assessment must be based on reliable measures by neurosurgeon and non-neurosurgeons. The mRS and iNPHGS by a surgeon and physiotherapists were not well corresponded. The FIM by physiotherapists and the iNPHGS by a neurosurgeon showed high improvement rate. Their changes on total, motor and cognition domains were well corresponded.

Thus, the FIM is suitable for assessment of shunt effectiveness in iNPH by non-neurosurgeons.

**Disclosure:** Nothing to disclose
EP4107

Comparative evaluation of functional MRI in patients with post-traumatic and amnestic mild cognitive impairment
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One of the main causes of cognitive impairment is Alzheimer’s disease. In addition, cognitive impairment may experience quite often as a consequence of craniocerebral trauma. At the same time, craniocerebral trauma is considered as a risk factor for a neurodegenerative process. Consequently, it may be necessary to the differential diagnosis of cognitive impairment specified etiology, especially in the early stages of the disease.

To identify specific areas of activation we conducted a comparative evaluation of the results of functional MRI (fMRI) in patients with mild cognitive impairment (MCI). Two groups were examined: 19 patients with post-traumatic MCI (with severe craniocerebral trauma in anamnesis), and 21 patients with amnestic MCI. Data processing was performed using SPM8 software. In the study we have used a specially developed specific cognitive paradigm.

Analysis of the results showed that patients with post-traumatic MCI were characterized by the presence of activations in the right superior frontal gyrus and supramarginal, 21 and 13 fields by Brodmann, the left middle temporal gyrus, 31 and 32 fields by Brodmann, as well as in the inferior frontal gyrus and thalamus from both sides. In patients with amnestic MCI activation was identified in the right superior and inferior temporal gyrus and gyrus parahippocampalis, left 21 field by Brodmann, as well as bilateral activation in the middle cingulate cortex.

Obtained results provide additional differential criteria of amnestic and post-traumatic MCI, and allow to clarify the pathogenesis of some symptoms observed in the structure of their neuropsychological profile.

Disclosure: Nothing to disclose

EP4108

Differences in routine clinical practice in early and late onset Alzheimer’s disease: data from the Swedish Dementia Registry (SveDem)
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Introduction: Due to age of onset, Alzheimer’s disease (AD) is divided into early onset (EOAD) or late onset (LOAD), but emerging data suggests that also the underlying pathology may be different. Whether differences in clinical care exist is less well investigated. We aimed to evaluate whether there are differences in demographics, diagnostic work-up and pharmacological treatment between EOAD and LOAD.

Methods: Data on patients with newly diagnosed EOAD (n=453) and LOAD (n=4599) was obtained from the Swedish dementia registry (SveDem). Logistic regression models were used to adjust for confounders including gender, cognitive decline and co-morbidity.

Results: The majority of patients with EOAD went through an extended diagnostic work-up including more technical investigations as well as assessments by neuropsychologists and speech therapists than patients with LOAD. The majority of EOAD and LOAD were in the mild stage of the disease when diagnosed. EOAD patients were treated with overall fewer medications but obtained treatment with cholinesterase inhibitors to a higher extent than those with LOAD, while there was no difference between the groups in antidepressant and antipsychotics use.

Conclusions: There are differences between EOAD and LOAD in diagnostic work-up and pharmacological treatment. An extensive diagnostic work-up should be recommended when EOAD is suspected.

Disclosure: Nothing to disclose
EP4109

Prevalence and safety aspects concerning the use of dietary supplements and herbal products among demented patients attending an outpatient clinic in North-Norway

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Introduction: Medical treatment options for dementia are scarce. Dietary supplements and herbal products (DSHEA), however, are often claimed useful for memory and mental health. Potential interactions with prescription drugs and other safety aspects concerning the use of such products in dementia are largely unknown.

Methods: The use of DSHEA among demented patients attending an out-patient memory clinic were registered by interview of the patient and a relative. Demographic data, the daily life situation and prescription drugs were also registered.

Results: 151 patients were included consecutively in 2011-2013. Mean age was 73 years and 61% were female. Mean MSSE-Nr score was 20. Sixty-two patients (46%) reported use of at least one DSHEA, with fish oils as the most frequently DSHEA used. The mean number of of prescribed medicines was four (range 0-17). Seven possible interactions between DSHEA and prescribed drugs were detected, of which three involved warfarin. Most patients reported help with administration of their prescribed drugs. However 61% of the patients using DSHEA reported no help with these products regarding administration. Ten % received help from home care, while the remaining received help from relatives. Seven patients who used DSHEA lived alone and had no home care.

Conclusions: Nearly half the patients used DSHEA. Clinical relevant interactions with prescription drugs can not be ruled out. Although most patients received help with the administration of prescribed drugs, few patients received help with DSHEA.

Disclosure: Nothing to disclose

EP4110

Evaluation of routinely used cerebrospinal fluid biomarkers in neuropathologically confirmed cases of human prion disease and other neurodegenerations – the Czech perspective

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Introduction: Cerebrospinal fluid (CSF) biomarkers are being widely used as an important diagnostic modality in differential diagnosis of dementia. Most widely used biomarkers are total tau (t-tau), phospho-tau (p-tau), amyloid-beta and protein 14-3-3 in the CSF. Their evaluation is important in differential diagnosis of Alzheimer’s disease and also in the differential diagnostic workup for rapidly progressive dementia including prion diseases. The aim of our study was to evaluate and compare the biomarker levels in the cohort of patients with neuropathologically confirmed prion disease or other neurodegenerative disorder.

Methods: Of a total of 45 CSF samples with neuropathologically confirmed diagnosis, 27 had prion disease and 18 other neurodegenerative disease. Neuropathologic evaluation was performed according to standardized protocols and the values of t-tau, p-tau and amyloid-beta were measured using commercial ELISA kits, protein 14-3-3 detection was performed by Western blot.

Results: Very high h-tau levels (>1200pg/ml) and 14-3-3 positivity are characteristic of prion diseases when compared to other neurodegenerations. We found no significant difference in the biomarker levels among different neurodegenerations.

Conclusion: Our observation of higher T-tau levels and protein 14-3-3 presence in the CSF in prion disease patients is in agreement with previous studies. The strength of our study is in the neuropathologically-based approach when only those patients with definite diagnosis of prion disease or other neurodegeneration with excluded concomitant neuropathology were included. The study was supported by Research Project Charles University in Prague, PRVOUK P26, GACRP303/12/1791 and grants NT12094-5 NT14145-3 from the Czech Ministry of Health.

Disclosure: Nothing to disclose
EP4111
Montreal Cognitive Assessment (MoCA) in mild cognitive impairment: correlation with cerebral perfusion in SPECT
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Introduction: The Montreal Cognitive Assessment (MoCA) is a brief cognitive screening instrument developed for detection of milder forms of cognitive impairment. Several cohort studies confirm its high sensitivity in the identification of MCI and mild AD patients. Our main objective was the evaluation of the relationship between the performance on the MoCA and regional cerebral blood flow (rCBF) measured by single photon emission computed tomography (SPECT), in Mild Cognitive Impairment (MCI).

Methods: We included 88 patients with MCI (amnestic single or multiple domains) according to Petersen criteria, extensively studied with comprehensive neuropsychological assessment, biomarkers and longitudinal evaluation (37% converted to dementia in 2 years). rCBF at inclusion was measured using Tc-99m hexamethylpropyleneamine oxime (HMPAO) and quantitative analysis normalized to cerebellum were measured in 20 zones and 90 areas (Broadmann areas) using NeuroGam-software. Elementary statistical analysis, t-Student test, and VisRed software, where used to analyze rCBF data.

Results: MCI group presented a significant hypo-perfusion (more than 1.5SD) comparatively to an internal-software control group, in posterior cingulate cortex (A23 e A24), left entorhinal cortex (A28) and temporoporal area (A38). We found significant negative correlations between MoCA total scores (mean value:18.97±4.637) and hypoperfusion in right caudate nucleus and angular gyrus. Orientation and Memory were the MoCA cognitive domains with strong correlations with hypoperfusion in Broadmann areas, namely the fusiform gyrus, angular gyrus and associative visual cortex.

Conclusions: Performance of MCI patients on the MoCA correlates with functional imaging, confirming sensitivity of the test to evaluate eloquent areas typically affected in AD.

Disclosure: Nothing to disclose

EP4112
Regional difference of Alzheimer’s disease and Parkinson’s disease associated with dementia using cerebral perfusion SPECT
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Introduction: Since patterns of cognitive dysfunction in mild Parkinson’s disease associated with dementia (PDD) are similar to those in mild Alzheimer’s disease (AD), it is difficult to accurately differentiate between these two types of dementia in their early phases using neuropsychological tests. The purpose of the current study was to investigate differences in cerebral perfusion patterns of patients with AD and PDD at the earliest stages using single photon emission computed tomography (SPECT).

Methods: We consecutively recruited 31 patients with mild PDD, 32 patients with mild probable AD and 33 age-matched healthy subjects. All subjects underwent 99m Tc-hexamethylpropyleneamine oxime perfusion SPECT and completed general neuropsychological tests.

Results: We found that both mild PDD and AD patients showed distinct hypoperfusion in frontal, parietal and temporal regions, compared with healthy subjects. More importantly, hypoperfusion in occipital and cerebellar regions was observed only in mild PDD.

Conclusions: The observation of a significant decrease in cerebral perfusion in occipital and cerebellar regions was observed only in mild PDD.

Disclosure: Nothing to disclose