Neuroimmunology

**P2803**

**Auto-antibodies in adult herpes encephalitis**

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Herpes encephalitis is the most common cause of non-endemic encephalitis and a cause of high mortality and morbidity. Even after anti-viral treatment, 30% of patients die and morbidity rate is high. Despite clinical recovery patients often present with chronic progressive damage of affected brain regions. These findings support the involvement of a virus-independent mechanism. Recently, anti-neuronal antibodies such as anti-N-methyl-D-aspartate receptor (NMDAR) and anti-voltage-gated potassium channel complex (e. g. CASPR2, LGI1) antibodies have been described in encephalitides with unknown cause. Anti-neuronal antibodies have not been tested systemically in viral encephalitides so far. Therefore, we tested 22 herpes simplex (HSE) and 12 varicella zoster encephalitis (VZE) patients for auto-antibodies against a spectrum of neuronal antigens. Applying cell-based assays (CBA) and radioimmuno-precipitation assays (RIA) we found that 9/22 HSE patients were positive for anti-neuronal antibodies: 4/22 were positive for anti-NMDAR, 1/22 for anti-CASPR2, 2/22 for anti-LGI1, 2/22 for anti-TAG and 2/22 for anti-VGKC antibodies. In the VZE cohort, 3/12 patients were tested positive by CBA: 1/12 for anti-NMDAR, 1/12 for CASPR2 and 1/12 for anti-TAG antibodies. All patients were negative for antibodies to aquaporin-4, glycine receptor (GLYR) and the intracellular antigen glutamic acid decarboxylase (GAD). We conclude that anti-neuronal auto-antibodies are present in virus mediated encephalitides, although the potential pathogenicity of the antibodies is unclear. This suggests that in addition to anti-viral treatments, immunosuppressive drugs such as corticosteroids may be helpful to improve the patient’s outcome and to minimize morbidity.

**P2804**

**Anti-NMDAr encephalitis in children and adolescents: a long-term follow-up in a French case series**

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**Introduction:** Since anti-NMDAr encephalitis’s first description in 2007 in women with ovarian teratoma, its clinical spectrum has grown to comprise children, adolescents, men and older adults, with or without tumour. Only one large series of children has been published with a short-term follow-up.

**Methods:** We systematically reviewed all anti-NMDAr positive patients diagnosed in the French Reference Center of Paraneoplastic Neurological Syndromes between October 2007 and November 2011. Out of 83 patients of all ages, detailed clinical data was obtained in 28 children and adolescents.

**Results:** Median age at onset was 12.4 years. Female-to-male ratio was 3:1. Prodromal symptoms were present in 10/18 assessable cases (mostly headache). The presenting symptom was mostly seizures (11/28). During disease evolution, 27 patients presented psychiatric symptoms, 27 cognitive impairment, 26 movement disorders, 25 seizures, 19 sleep disorders, 15 decreased level of consciousness, 11 dysautonomia. Brain MRI was abnormal in 15/28 cases, EEG showed signs of encephalopathy in all cases. CSF inflammation was observed in 22/27 assessable cases. No tumour was detected after extensive screening. Patients received corticosteroids (24), immunoglobulins (25), plasma exchanges (12), rituximab (19), cyclophosphamide (4), azathioprine (4). After a mean follow-up of 14 months 1 patient died, 1 patient had full recovery under anti-epileptics, 1 patient had motor symptoms and 25/28 patients had cognitive sequellae of various severity, while 4 patients had a relapse.

**Conclusion:** Anti-NMDAr encephalitis in children and adolescents can be present without a concomitant tumour. Although all patients were intensively treated by immunomodulators or immunosuppressors, cognitive sequellae are frequent.
P2805

Non-muscle myosin light-chain kinase mediates microglial migration induced by HIV Tat: involvement of β1 integrins

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Introduction: HIV Tat released from HIV-infected cells has been shown exhibiting chemotactic activity. Activated microglia are a hallmark feature of HIV-associated neurological disorder (HAND). These cells can migrate to the signal elicited by HIV Tat released from infected cells. We hypothesized that the microglial adhesion/migration mediated by Tat will involve actin rearrangement and the activation of its upstream non-muscle myosin light chain kinase (MYLK) and integrins.

Methods: Microglial migration was assessed by both Boyden and Dunn Chamber. Role of Cdc42 was assessed by GLISA. F-actin polymerization was examined by palladin staining and flow cytometry. HIV Tat was stereotactically injected in the mice hippocampus followed by transplantation of AAV-GFP transduced mice microglia in the corpus callosum.

Results: Intra-hippocampal injection of HIV Tat1-72 into mice resulted in migration of AAV-GFP transfected microglia to the Tat-injected site. Molecular mechanisms of this process involved Tat-mediated activation of VEGFR1 receptor, leading to inside-out activation of MYLK & β1 integrin, resulting subsequently in outside-in activation of the downstream Pyk2, Src, and Cdc42. This ultimately culminated into actin rearrangement and the ensuing migration of microglia.

Conclusions: Our findings for the first time have identified two novel phenomena: a) RGD-independent activation of β1 integrin by HIV Tat and, b) involvement of MYLK in Tat-mediated microglial migration.

P2806

Progressive multifocal leukoencephalopathy in a patient with transitory lymphopenia

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Progressive multifocal leukoencephalopathy (PML) is a rare disease due to reactivation of the Polyomavirus JC (JCV) in immunosuppressed subjects, some of them developing the immune reconstitution inflammatory syndrome (IRIS) when treated for the PML cause. We document temporary T-cell lymphopenia (TTL) triggering PML in an otherwise immunocompetent patient, diagnosed at PML-IRIS stage. This 64-year-old man complained of progressive speech difficulties with superimposed acute symptoms worsening. Neurological examination noticed extensive cognitive disorders and somatic deficits slightly lateralized to the right side, corresponding to a large left fronto-parieto-temporal, gadolinium-enhancing subcortical lesion. However, extensive blood and CSF workup was inconclusive (auto-immune antibodies, infection, including undetectable JCV DNA twice in the CSF). There was an unexplained CD4+, CD8+ T and B lymphopenia with normal IgG, M and A levels. A stereotactic cerebral biopsy established diagnosis of PML-IRIS (>600,000 JCV DNA copies/ml and prominent inflammatory features within the lesion). Without any therapeutic intervention, the patient progressively improved 4 months later, in parallel with spontaneous CD4+ and CD8+ and total lymphocytes normalization. In the absence of any other cause, we concluded that temporary T-cell lymphopenia was able to trigger PML, probably due to a benign viral infection. A strong JCV-specific cellular immune response presumably lowered JC viral load and/or increased its clearance in the CSF, most probably explaining the good clinical outcome. In conclusion, this case confirms that even a transitory immunosuppression is capable to trigger PML with spontaneous IRIS. Despite acute neurological deterioration this IRIS correlates with a favourable outcome.
P2807
The inflammatory role of TNF-α in experimental auto-immune neuritis is mediated by its receptor 1 to induce activated macrophages with a pro-inflammatory phenotype (M1)

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Aim: To further clarify TNF-α’s mechanism of action and to explore the potential role of TNF-α receptor (TNFR)1 as a therapeutic target in experimental auto-immune neuritis (EAN), an animal model of human Guillain-Barré syndrome (GBS).

Methods: EAN was induced by immunization with P0 peptide 180-199 in TNF-α knockout (KO) mice and anti-TNFR1 antibodies were used to treat EAN. Particularly, the effects of TNF-α deficiency and TNFR1 blockade on macrophage functions were investigated.

Results: The onset of EAN in TNF-α KO mice was markedly delayed compared to wild type (WT) mice. From day 14 post-immunization on the clinical signs of TNF-α KO mice were significantly milder than those of their WT counterparts. We then blocked TNFR1 by using anti-TNFR1 antibodies. The clinical severity of WT mice treated with TNFR1 antibodies was less severe than in the control WT mice receiving PBS. Nevertheless, no difference with regard to the clinical signs of EAN or inflammatory infiltration in cauda equina was seen between TNF-α KO and WT mice with EAN after blockade of TNFR1. TNF-α deficiency induced an anti-inflammatory phenotype of macrophages (M2) characterized by reduced production of interleukin (IL)-12 and nitric oxide (NO), and enhanced production of IL-10. Increased ratio of regulatory T-cells (Tregs) and reduced production of interferon (IFN)-γ in infiltrating cells in cauda equina, and elevated levels of IgG2b antibodies against P0 peptide 180-199 in sera were found in TNF-α KO mice with EAN.

Conclusion: TNF-α exacerbates EAN via TNFR1 by inducing classically activated macrophages (M1).

P2808
Role of NADPH oxidase 2-dependent redox signal in bradykinin-induced MMP-9 expression in brain astrocytes

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Matrix metalloproteinase-9 (MMP-9) plays a crucial role in pathological processes of brain inflammation and injuries. Moreover, bradykinin (BK) induces the expression of several inflammatory proteins in brain astrocytes. Recent studies have suggested that increased oxidative stress is implicated in the brain inflammation and injury. Herein we explored the roles of redox signals in BK-induced MMP-9 expression in brain astrocytes. In the study, we first demonstrated that BK induces MMP-9 expression via reactive oxygen species (ROS)-dependent manner in cultured brain astrocytes (in vitro) and animal brain tissue (in vivo). Next, BK-induced MMP-9 expression is mediated through a Ca2+-mediated PKC-alpha linking to p47phox/NADPH oxidase 2 (Nox2)/ROS signalling pathway. Nox2-dependent ROS generation led to activation and up-regulation of the downstream transcriptional factor AP-1 (c-Fos and c-Jun), which bound to MMP-9 promoter region, and thereby turned on transcription of MMP-9 gene. Functionally, BK-induced MMP-9 expression enhanced astrocytic motility. This is the first study to demonstrate that BK-induced redox (ROS) signal may play a critical role in brain inflammation and injuries. Taken together, these results suggested that in rat brain astrocytes (RBA-1), activation of Nox2-mediated ROS generation by a Ca2+-dependent PKC-alpha event enhancing AP-1 (c-Fos/c-Jun) pathway is essential for BK-induced MMP-9 up-regulation and cell motility.

P2809
Abstract cancelled
P2810

Viral load, cytokine storm, TNF-α and TNF-α promoter polymorphism as possible predictors for disease progression in Japanese encephalitis

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Japanese encephalitis (JE) is an important arboviral infection of public health concern. JE manifests with a self-limited febrile illness to severe encephalitis. As the disease pathogenesis is poorly understood, study on cytokine profiles (Th1 and Th2), viral load on disease severity and TNF-α promoter polymorphism as host genetic makeup were undertaken. 227 patients with acute encephalitic syndrome, 126 febrile illness suspected of JE and 79 apparently healthy individuals as control were enrolled. JE cases were diagnosed with IgM captured ELISA and RT-PCR. 88 (54.7%) encephalitis patients, 50 (39.7%) febrile illness cases were diagnosed as JE and 50 (63.3%) controls had JE specific IgG antibodies. Bioinformatics analysis revealed JEV genotype III as circulating strain and a novel S227T mutation in domain III of E gene. Significantly high viral load was detected in severe JE patients than in those with milder encephalitis (43,349 vs. 8,721 mean copies/ml). Interestingly, significant levels of TNF-α (>55pg/ml cut-off) and IL-6 (>370pg/ml cut-off) in encephalitis due to JE and IFN-γ in febrile JE patients without encephalitis were observed. Th1 shift (IFN-γ /IL-4: >1) was observed in encephalitis patients. TNF-α promoter polymorphism analysis revealed significant distribution of -308A and -863C alleles in encephalitis group more so among 7 out of 9 patients died from this group having the same allelic distribution. Th1 cytokine shift; higher levels of viral load, IL-6 and TNF-α and significant distribution of -308A and -863C alleles of TNF-α promoters are possible major contributors of severity and mortality among Japanese encephalitis cases.

P2811

Intrathecal transplantation of adult neural stem/precursor cells dampens the effector phase of experimental auto-immune encephalomyelitis

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Introduction: Neural stem/precursor cell (NPC) transplantation ameliorates disease severity in experimental auto-immune encephalomyelitis (EAE) through bystander neuroprotective and immunomodulatory effects. We investigated how NPCs directly transplanted in the cerebrospinal fluid interfere with the CNS-infiltrating immune effector cells that sustain neuroinflammation.

Methods: Chronic EAE was induced in C57 Bl/6 mice by immunization with the MOG 35-55 peptide. At the peak of the disease, 20 mice per group were transplanted in the cisterna magna by stereotaxic injection of GFP-labelled adult NPCs or vehicle. The in vivo characterization of transplanted NPCs was assessed by immunofluorescence and ex vivo analysis of CNS inflammatory infiltrate was performed by flow cytometry.

Results: After 40 days post-immunization (dpi), transplanted NPCs persisted almost exclusively within the perivascular inflammatory infiltrate and around 70% retained an undifferentiated phenotype. NPC-transplanted mice showed a persistent amelioration of disease severity when compared with sham-treated mice in terms of clinical score (1.1±0.25 improvement at 80 dpi p<0.02), demyelination (57%, p<0.05) and axonal loss (750%, p<0.02). Moreover, at 40 dpi we observed in NPC-transplanted mice a quantitative reduction of infiltrating myeloid dendritic cells (58.92% reduction, p<0.01), macrophages (34.02% reduction, p<0.01) and T-cells (24.97% reduction, p<0.05), in particular Th17 (35.98% reduction, p<0.01) and Th1 (36.62% reduction, p<0.01) effector cells.

Conclusion: This work confirms the efficacy of intrathecal transplantation of adult NPCs in ameliorating disease severity in experimental multiple sclerosis and suggests that transplanted NPCs target the CNS-restricted pathogenic phase of neuroinflammation.
P2812

Clinical features, neuroimaging findings and pathological characteristics of 45 patients with tumefactive demyelinating lesions

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Objectives: To retrospectively explore the clinical features, neuroimaging findings and pathological characteristics of patients with tumefactive demyelinating lesions (TDL) confirmed by histopathology.

Methods: A total of 45 cases (24 males and 21 females) with histologically confirmed TDL (43 cases with the brain type and 2 with the spinal cord type) were reviewed.

Results: The mean onset age was 34.6±12.7 (range 6-69) years. 40 cases were followed-up for a median duration of 38 months. Two patients died of post-operative complications and the other 3 patients were lost to follow-up. 35 out of 40 TDL patients showed a monophasic clinical course. Headache, indifference and hypomnesis were the most common initial presentations. Abnormality rate of myelin basic protein (MBP) in TDL patients were high. 34 patients showed hypodense round lesions in conventional CT scanning. TDL in most cases presents as low signals in MRI-T1WI and high signals in MRI-T2WI. In 41 patients receiving contrast-enhanced MRI scanning, 27 cases showed open-ring enhancement, 5 ring enhancement, 3 asymmetric dotted enhancement, 3 diffused even enhancement, and 6 no enhancement. Furthermore, high signals appeared in 29 cases with DWI and 22 with FLAIR. The typical pathological changes were demyelination, perivascular inflammatory cells infiltration and gliosis. Creutzfeldt cells were occasionally found in some patients.

Conclusions: TDL is a distinct demyelinating disease entity, with its specific clinical and neuroimaging features. TDL showed hypodense lesions in conventional CT scanning. Patients with hyperdense lesion in cranial CT scanning could not be TDL.

P2813

The 'Immunomodulation and Multiple Sclerosis Epidemiology' (IMSE) study: a Swedish nationwide pharmaco-epidemiological and genetic study focused on long-term safety and efficacy of natalizumab (Tysabri)

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Natalizumab is an effective treatment improving quality of life in people with MS. However, the safety/efficacy in a real-world setting is important to monitor. In August 2006 a post-marketing surveillance study started to monitor long-term effectiveness, adverse events (AEs) and identification of genes and biomarkers involved in the development of severe MS. Patients were registered in the “Swedish Multiple Sclerosis registry” from 46 centres and evaluated every 6 months. AEs, extended disability status scale (EDSS), multiple sclerosis severity scale (MSSS), symbol digit modalities test (SDMT), multiple sclerosis impact scale (MSIS-29) and relapses were recorded. Patient blood samples were taken at baseline, 6, 12, 24 months after treatment. Until February 2012; 1,740 patients were included of which 81.1% were diagnosed with RRMS. Of all, 24.6% stopped the treatment and the main reason was pregnancy. Serious AEs were rare (2.6%) but included 5 cases of progressive multifocal leukoencephalopathy (PML, 0.3%) and 8 deaths (0.5%). In patients treated for ≥4 years (n=316) significant improvements were shown in; MSSS (-31.3%), SDMT score (+18.0%), MSIS-29 physical/psychic scores (-13.0% and -17.9%), while EDSS increased slightly (+8.7%), Mean number of relapses was 3.68 before treatment and during treatment the mean number of relapses had dropped to 0.55 under the entire observation period, i.e.<0.2 relapses/year. The Swedish Multiple Sclerosis registry proved to function well as a post-marketing drug surveillance platform, providing long-term data regarding drug effects AEs. Natalizumab is generally well tolerated with sustained efficacy, though the risk of PML is still an important concern.
P2814

The significance of NMO-IgG positivity in neuromyelitis optica spectrum disorders: preliminary results

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Introduction: Neuromyelitis optica (NMO) or Devic’s disease is a rare inflammatory and demyelinating disorder of the central nervous system (CNS) characterized by recurrent attacks of optic neuritis (ON) and longitudinally extensive transverse myelitis (LETM), which is distinct from multiple sclerosis (MS). Testing for NMO-IgG is recommended for the patients with classic NMO, transverse myelitis with longitudinally extensive spinal lesion, severe or relapsing ON. The aim of our study is to assess the frequency, syndrome specificity, diagnostic relevance of NMO-IgG in NMO and NMO-spectrum disorders.

Methods: We investigated NMO-IgG for the following groups: 1) typical NMO, 2) ON without typical MS brain lesions 3) transverse myelitis (TM), 4) MS patients. Serum samples were collected from 28 patients and tested for NMO-IgG by using indirect immunofluorescence method and study group included; 7 NMO, 8 ON (two of them recurrent ON), 4 TM, 9 MS patients.

Results: NMO-IgG positivity has been detected in 57.14% of NMO patients and 25% of TM patients. Neither patients with ON nor with MS did have positive NMO-IgG antibodies.

Conclusions: The identification of NMO-IgG and aquaporin-4 as a target antigen makes NMO as a first defined inflammatory, demyelinating disorder of the CNS. There are different methods for detection of NMO-IgG that facilitating early diagnosis and appropriate treatment. Our preliminary results showed that the rate of the NMO-IgG positivity was lower in Turkish cases than in other populations.

P2815

Downbeat nystagmus: a case report with anti-GAD antibodies, auto-immune thyroiditis and late onset diabetes

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Introduction: Auto-antibodies to glutamic acid decarboxylase (anti-GAD Abs) have been found in a variety of neurological and endocrine disorders.

Methods: Case description of a 55-year-old woman with a past history of auto-immune thyroiditis, who presented with insidious onset oscillopsia, dizziness and downbeat nystagmus. We review the clinical course and imaging studies, serological and immunological findings at periphery and cerebrospinal fluid (CSF).

Results: Markers of paraneoplastic cerebellar ataxia and collagen diseases were negative apart from high titre of anti-TPO Abs (126.31U/ml). She had high levels of serum anti-GAD-Abs (>20,000U/ml). Fasting plasma glucose and OGTT were pathological, HbA1c- 9.2. Brain and cerebral CT / MRI, thoracic and abdominal CT were normal. CSF had positive oligoclonal bands and showed intrathecal synthesis of GAD-Abs. Treatment with 3.4 aminopyridine, improved her nystagmus partially, but not the dizziness and vomiting. Later on the clinical course cerebellar symptoms were added: heel-shin dysmetria, dysdiadochokinesis. Intravenous immunoglobulin (IVIg) was administered with good therapeutic effect.

Conclusion: In primary auto-immune cerebellar ataxia, additional auto-immune disease may precede or follow the development of ataxia. If cerebellar ataxia with an auto-immune mechanism is suspected, it is worth considering immunomodulatory treatment, including IVIg.
P2816

Two unusual cases of non-paraneoplastic auto-immune encephalitis

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Introduction: Auto-immune encephalitides are being increasingly recognized as important (and potentially reversible) non-infectious causes of an encephalitic syndrome. In contrast to paraneoplastic encephalopathic syndrome these antibodies target the extracellular domain of the neuronal protein & their presence usually indicates the possibility of successful immunotherapy.

Objective: The clinical presentations of auto-immune encephalitis can be varied and non-specific. However there are some consistent discriminating features reported in the literature albeit with an atypical indolent clinical course. We report two unusual cases of antiVGKC mediated encephalitis. Both of which responded to immune modulatory therapy.

Case report: Case 1 presented with faciobrachial dystonic seizures (video), hyponatraemia and cognitive impairment. Consistent with typical features of anti-voltage gated potassium channel antibody disorder. The clinical course was protracted and response to standard immunotherapy (combination of Steroids, Immunoglobulin & Plasma exchange) was poor, however response to Rituximab was substantial. In this case VGKC were raised >4,000 and NMDA receptor antibodies were also markedly raised. Case 2 presented with a one-year history suggestive of frontotemporal dementia (FTD) associated with a dyskinetic movement disorder and seizure syndrome. Antibodies to neuronal voltage-gated potassium channels (VGKC-Abs) were >4,000 and response to immunomodulatory therapy was prompt.

P2817

Toll-like receptor 2 deficiency ameliorates acute inflammatory demyelinating polyneuropathy by inducing alternatively activated macrophages (M2)

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Introduction: Toll-like receptors (TLRs) are a group of pattern recognition receptors sensing exogenous and endogenous detrimental signals. Activation of TLRs through the MyD88-dependent or MyD88-independent pathway triggers T helper 1 oriented auto-immune responses by inducing production of IL-12 and TNF-alpha. TLR2 is one of the most extensively studied members of the TLR family and has been associated with many auto-immune disorders.

Methods: Experimental auto-immune neuritis (EAN) was induced by immunization with P0 peptide 180-199 in TLR2 knockout (KO) mice and in C57BL/6 mice as wild type (WT) controls. The effects of TLR2 deficiency on the clinical course of EAN and the functions of T-cell and macrophages were studied.

Results: Toll-like receptor 2 deficiency remarkably ameliorated EAN. From day 14 post-immunization, the clinical signs of TLR2 KO mice were significantly milder than those of their WT counterparts. Upregulated expression of TLR2 was detected on the infiltrating macrophages in cauda equina of EAN WT mice and was correlated with the clinical scores. Although TLR2 deficiency did not alter the proliferation of lymphocytes in response to either antigenic or mitogenic stimulation, it induced an anti-inflammatory phenotype of macrophages (alternatively activated macrophage, M2) characterized by reduced production of interleukin (IL)-12 and nitric oxide (NO), and enhanced production of IL-10.

Conclusion: Toll-like receptor 2 deficiency ameliorates EAN by inducing alternatively activated macrophages (M2).
P2818
Hypothalamic proline rich polypeptide Galarmin (PRP-1) regulates metalloproteins activities at lypopolysachardide and methicillin-resistant Staphylococcus aureus induced oxidative damage
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We investigated the antioxidant and regulatory effect of the hypothalamic proline-rich polypeptide Galarmin (PRP-1) on the level and activity of metalloproteins of antioxidant activity (MAA) (Cu, Zn-SOD, Mn-SOD, catalase) and NADPH depending O2- – producing activity of metalloproteins of pro-oxidant activity (MPA) (the isoforms of NADPH-oxidase) during the oxidative stress induced by intraperitoneal (i.p.) lypopolysacharade (LPS) injection in rats (0.5mg/kg) and methicillin-resistant Staphylococcus aureus (MRSA) i.p. infection in mice (6x108CFU/mice) in the presence or absence of Galarmin treatment (25µg/kg i.p. for rats; 1µg/mice i.m.). The fractions of MAA and MPA from blood serum and tissues (bone marrow, liver, kidney and spleen cells) were analysed by the method of gel-filtration and ion-exchange chromatography. The statistical analysis was performed employing Students’ test, considering statistically significant value of p<0.05. It has been shown that Galarmin brought the levels and activities of the MAA and MPA to the norm and indicates the anti-stressory effect by decrease of NADPH depending O2-producing activity of Nox isoforms, mostly serum isoform Nox. Therefore we concluded that Galarmin manifests both antioxidant and anti-stressory activity during the inflammatory reactions induced by LPS and MRSA.

P2819
Progressive amnesia and temporal lobe epilepsy in a young patient - promptly consider auto-immune limbic encephalitis
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Introduction: Limbic encephalitis associated with auto-antibodies directed against cell-surface neuronal antigens is being increasingly recognized. Patients with antibodies against VGKC-complex typically present with acute or subacute onset of amnesia, temporal lobe seizures and neuropsychiatric symptoms. Serum hyponatremia and MRI high signal in mesial temporal lobes are characteristic features.

Case report: A 43-year-old male patient, without relevant past medical or family history, presented with a 9-month history of progressive memory loss, mainly affecting episodic memory, and altered behaviour, that ultimately disabled him for work. Previous investigation included brain 1.5T MRI (considered to be normal) and EEG (right temporal paroxysmal activity). General physical and neurological examination was unreliable except for temporal-spatial disorientation. Neuropsychological evaluation revealed severe episodic memory impairment and was positive for dementia. Blood and CSF analysis and 3T brain MRI were normal and video-EEG documented one left electro-clinical temporal lobe seizure. Auto-immune encephalitis was considered and high titres of antibodies against VGKC-complex were identified (2,759 pM). High dose intravenous methylprednisolone was started, followed by oral prednisolone 1mg/kg/day. 3 months later, because of obsessive behaviour development and the absence of significant cognitive improvement, monthly intravenous immunoglobulin (IVIG) was started. Neuropsychological evaluation after three IVIG cycles did not reveal significant improvement and plasmapheresis was performed.

Conclusion: It is essential to consider auto-immune encephalitis in the differential diagnosis of patients presenting with amnesia, psychological disturbance and seizures, even in the presence of normal MRI and serum sodium levels. Early diagnosis and treatment is crucial as it may dramatically improve patient outcomes.
P2820
A case of rheumatoid meningitis: neurological manifestation and pathological findings
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Introduction: Rheumatoid meningitis, one of the most severe complications of rheumatoid arthritis, presents various symptoms such as headache, confusion, loss of consciousness, seizure, fever, and focal neurological deficits.

Case report: A 63-year-old man with the history of rheumatoid arthritis presented with intermittent left leg weakness, seizures and later developed fever and confusion. Brain MRI demonstrated leptomeningeal enhancement at the right fronto-parietal area. The patient’s EEG finding shows bifrontal and independent right frontal 5-6 Hz rhythmic waves. Brain biopsy revealed multifocal suppurative inflammation. Gross finding shows suppurative dural infiltration in right frontal lobe. Microscopic findings show lymphocytic or plasmacytic infiltration, multinucleated giant cell and neutrophilic infiltration. After aggressive immunosuppressive treatment, he has gradually recovered along with a much improved MRI finding.

Conclusion: Although rheumatoid meningitis is a rare disease, it can cause permanent neurological deficit. In patients with history of rheumatoid arthritis, it is important to detect neurologic signs earlier. To confirm the diagnosis, brain MRI and brain biopsy are valuable.

P2821
A case of paroxysmal dysarthria-ataxia in idiopathic rhombencephalitis
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Introduction: Paroxysmal dysarthria-ataxia (PDA) is a rare neurological condition due to ephaptic transmission, generally appearing in multiple sclerosis patients characterized by transient (few seconds), stereotyped attacks of slurred speech usually accompanied by ataxia, appearing many times a day.

Case: We report a case of a 69-year-old woman affected by idiopathic rhombencephalitis that began 16 months earlier and presented three remitting-relapsing acute episodes characterized by the combination of hemi-ataxia and ophthalmoplegia, all responsive to high dose steroids (methylprednisolone 1gx5d). A new lesion in brainstem was documented on MRI T2-sequences at each episode. Interestingly, the third episode was associated with an enhancing lesion in the pons-midbrain tegmentum sparing an oval central area caudal to the red nuclei. The fourth attack was characterized clinically by pure PDA associated with a MRI lesion involving exactly this midbrain area. Steroids were not effective. No electrical correlates were shown by video-EEG and high-density-EEG registrations. Remission was achieved in 2 weeks by lamotrigine (50mg). Our laboratory blood and CSF investigations ruled out multiple sclerosis, Behçet’s disease or other systemic haematological or rheumatologic auto-immune diseases.

Conclusions: The peculiarity of this case consists of: its rarity (the third case of PDA not associated with multiple sclerosis); its exact anatomical localization by MRI (involvement of the brachia conjunctiva); its responsiveness to lamotrigine.
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Physostigmine and neostigmine reduce the increased expression of IL-1beta in the hippocampus and cortex after surgery combined with LPS-treatment

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Objectives: Post-operative cognitive dysfunction (POCD) is characterized by the impairment of cognitive function following surgery. Tissue injury during surgery is linked to the release of a variety of pro-inflammatory cytokines. The cholinergic anti-inflammatory pathway is a neurohumoral mechanism that plays a prominent role by suppressing the innate inflammatory response. Treatments with acetylcholinesterase inhibitors enhance cholinergic transmission and may act as anti-inflammatory agents. The proposed project is designed to test the mode of action of acetylcholinesterase inhibitors physostigmine and neostigmine in rats undergoing major surgery as a new strategy to prevent neuroinflammation and POCD.

Methods: Adult Wistar rats underwent surgery alone or combined with LPS-treatment in the presence or absence of physostigmine or neostigmine. The gene expression of IL-1beta, TNF-alpha and IL-10 was measured after 1h, 24h, 3d and 7d via Real-Time PCR. The protein expression of IL-1beta, TNF-alpha and IL-10 was detected by Western blot analysis or Cytometric Bead Array.

Results and conclusions: Surgery combined with LPS-treatment led to increased IL-1beta gene expression and consequently protein upregulation in the hippocampus, cortex and spleen after 1 and 24h and was significantly reduced by physostigmine and neostigmine. Furthermore, surgery combined with LPS-treatment caused increased gene- and protein expression of TNF-alpha and IL-10 in the spleen and plasma. Physostigmine and neostigmine significantly reduced TNF-alpha expression whereas IL-10 level was upregulated. Acetylcholinesterase inhibitor reduces the pro-inflammatory response after surgery combined with LPS-treatment in the hippocampus and cortex and may represent a tool to interrupt the pathogenesis of POCD.

P2823

Paraneoplastic cerebellar degeneration associated with diffuse large B-cell lymphoma and anti-VGCC antibody

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Introduction: Paraneoplastic cerebellar degeneration (PCD) is one of the most frequent paraneoplastic neurologic syndromes appearing as an auto-immune reaction to an underlying malignancy.

Case report: A 71-year-old man was admitted with subacute, progressive truncal and limb ataxia, dysarthria and nystagmus. Routine blood analyses revealed slightly elevated CRP, decreased vitamin B-12 and anaemia. Further extensive investigations, including tests for infections, brain and spinal CT scan, thoracic and abdominal CT scan were unremarkable except for a benign arachnoid cyst of the posterior fossa. CSF analysis showed mild pleocytosis, oligoclonal bands and raised IgG-index. Brain MRI was initially normal but demonstrated cerebellar atrophy in the later stage. A broad panel of paraneoplastic serology tests revealed positive result for P/Q- type voltage-gated calcium channel antibody. Whole-body 18F-fluorodeoxyglucose-positron emission tomography showed high accumulation in the gastric wall and suspicion of metastases in the thoracic wall and peritoneum. Gastroscopic biopsy disclosed extranodal diffuse large B-cell lymphoma with Helicobacter pylori positivity. No clinical or electrophysiological signs of myasthenic syndrome were present. The patient was treated with chemotherapy and radiation followed by regression of the gastric lymphoma and plasmapheresis were given however without improvement in neurological symptoms.

Conclusion: Attention is brought to the presentation of a new combination of classic paraneoplastic syndrome and associated tumour and antibody: paraneoplastic cerebellar degeneration associated with gastric diffuse large B-cell lymphoma and P/Q- type voltage-gated calcium channel antibody.
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Non-paraneoplastic, auto-immune encephalitis with anti-AMPA receptor antibodies associated with pernicious anaemia
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SPECT study in patients with auto-immune encephalitis without MRI abnormalities
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Leucin-rich glioma inactivated 1 (LGI1) antibody limbic encephalitis: a case report
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P2827
Opsoclonus myoclonus syndrome as a result of paraneoplastic syndrome
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Role of Chlamydia pneumoniae IgG antibody in ischemic stroke subtypes: data form a tertiary care center
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Abstract cancelled

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Neuroimmunological features of protection of chronic cerebral ischemia
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Case report of Nezelof syndrome
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Concomitance of myasthenia gravis with other auto-immune diseases
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P2833
The clinical outcome of severe Guillain-Barré syndrome with and without immunotherapy
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Remitting immune encephalitic lesions in a case of common variable immunodeficiency syndrome
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The specific prophylaxis influence on severity and immune genesis of tick-born encephalitis (TBE)
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Interchangeability between human immunoglobulins in neurological diseases
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Neuroimmune aspects of chronic cerebral ischemia
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P2839
Structure of the central nervous system, optic nerve and immune system after induction of demyelination and remyelination
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Neuro-psycho-Behçet’s misdiagnosed as somatoform disorder: a case report
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Anti-N-methyl-D-aspartate receptor encephalitis in Korea
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Immunoregulation of CD4+ T-cells by Fasudil in experimental auto-immune encephalomyelitis
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A retrospective study on the outcome of plasmapheresis in Guillain-Barré syndrome patients admitted at the Philippine general hospital from 2006-2010
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Pseudo tumour cerebri in an SLE patient
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