Accepted Abstracts

Neuroimmunology 2017

4th International Conference on

NEUROLOGY AND NEUROIMMUNOLOGY

September 18-19, 2017 | Embassy Suites by Hilton,
Dallas Park Central Area, Dallas, USA

J Neurol Neurosci, 8:5
DOI: 10.21767/2171-6625-C1-003

Who will guard; the guards themselves?

Andrew G MacLean, Joseph Ramsey, Olivia Purcell, Kim M Lee and Kevin B Chiu
Tulane University, USA

Background: Astrocytes have long been established as sentinels for infection. Glial activation has downstream effects on the blood-brain barrier and neurons. However, for many years, astrocyte activation following host infection was essentially limited to "astrogliosis", with the occasional addition of hypertrophy or atrophy. More recently, it has become possible to quantify the degree to which astrocytes are activated, and to discern which parameters are important for astrocyte function.

Methods: To determine how infectious agents alter astrocyte activation, we "mined" the archives at Tulane National Primate Research Center to find matched tissues from macaques infected with SIV (the parental virus of HIV), Chikungunya, Dengue and *Brucella.* Paraffin embedded cortical tissues were cut at 6 µm thickness and stained for GFAP and Toll-like receptor 2 for morphometric analyses and innate immune activation, respectively. Morphometric analyses were performed using Neurolucida software. Routine measures included cell body area, total arbor, arbor volume, number of dendrites, bifurcations, process endings and modified Sholl analyses.

Results: Bacterial infection (with *Brucella melitensis*) induced increases in all the parameters indicated above. In contrast, lentiviral infection induced decreases in the measured parameters, with the exception of cell body area in white matter, although that only occurred in animals with active encephalitis. Two closely associated flavi viruses, Chikungunya and Dengue, produced very different effects on the astrocytes. Whereas Dengue infection induced increases in all the parameters in white matter, Chikungunya induced decreases in bifurcations and tips, with increases in process volume in grey matter. Only cell body area was increased in white matter.

Discussion: Astrocytes respond rapidly to host infection. While it is not hugely surprising that glia respond differently to bacteria and viruses, what was surprising was that even very closely associated viruses induce different responses in astrocytes. We are currently generating software to differentiate astrocytes based on morphometric data.

e: amaclean@tulane.edu

J Neurol Neurosci, 8:5
DOI: 10.21767/2171-6625-C1-003

Multiple sclerosis: what we know, what we believe and what we don't know about the immunology of the disease(s)

Robert M Herndon
Mississippi State University, USA

Despite an extensive search for viruses related to multiple sclerosis (MS) and the isolation of multiple agents from MS brain specimens, none have been clearly tied back to the disease as causative agents. It is clear that Epstein-Barr virus (EBV) is important in its pathogenesis but it does not appear to be, in and of itself, causative. It has been shown that some of the oligoclonal bands seen in the spinal fluid are directed against EBV antigens but the evidence of the presence of the virus in the lesions is controversial and the best evidence seems to indicate that it is not present in the nervous system. Herpes VI has been found in some MS lesions and may play a role in some cases. Anti-herpes drugs appear to be helpful based on some phase II trials data but no real phase III trials have been done and the phase II trials were too small to clearly establish the benefit though there was a strong trend that suggested a larger trial was warranted. Additionally, there is good evidence that epitope spreading is an important factor in disease activity.

e: rherndon@umc.edu

Notes:

J Neurol Neurosci, 8:5
DOI: 10.21767/2171-6625-C1-003

Tumor necrosis factor receptor 1 and 2 (TNFR1/R2) deletion provoke inflammatory chemokines, cytokines and pain related hypersensitivity

Helieh S Oz
UK Medical Center, USA

Chronic inflammation of mucosal surface is an aberrant immune response to different chemical, environmental insults as well as luminal microbial which generate an array of cytokine and chemokines and oxygen radicals leading to tissue destruction and loss of function, as noted in pancreatitis, hepatitis, inflammatory bowel diseases (IBD), periodontitis, arthritis and temporomandibular joint disorders (TMJD). Patients with TMJD and arthritis often have a combined etiology of hereditary and microenvironmental factors contributing to joint pain. Multiple clinical and animal studies have proven "dual-hit phenomenon" as inflammatory insults to initiate chronic response in joints and in other related as well as unrelated organs. As, the initial inflammatory insult primes the immune system, the succeeding insult/s amplify/s deleterious responses. Pro-inflammatory cytokine, tumor necrosis factor α (TNFα) up-regulates various inflammatory markers, cytokines and chemokines to initiate acute and chronic stages of inflammation and pain related sensation in patients and model for pancreatitis, hepatitis and IBD, as well as neuropathy. TNFα is released mainly by activated macrophages, astroglia, microglia, CD4+ lymphocytes, natural killer cells, and neurons. The biological action of TNFα is through two gene family receptors, TNFR1 and TNFR2. Dysregulation of TNFα contributes to development of colitis, hepatitis, pancreatitis, headache, periodontal, temporomandibular and neuropathic pain. Trigeminal neuropathic pain is common following trigeminal nerve damage post-surgical procedures and maxillofacial injuries. Soluble TNFR1 and R2 neutralize circulating TNFα to alleviate pain related responses such as allodynia, hyperalgesia or peripheral nerve injuries. Murine with genetic deletion of TNFα receptors (TNFR1/R2 deficient) develop severe chronic inflammatory symptoms including pancreatitis and orofacial trigeminal inflammatory compression (TIC) nerve injuries compared in WT animals. In addition, TNFR1/R2 deficient animals after recovering from initial inflammatory insult, such as knee joint arthritis or unilateral into temporomandibular joint (TMJ), when exposed to second but unrelated, colonic inflammatory, insult, develop recrudescence chronic secondary hypersensitivity which continued for over 4-6 months duration of studies. Analysis of proteomic profiling at multiple time points identified several altered levels of inflammatory cytokines and chimokines. This presentation will discuss in detail relationship between TNFα and its receptors to provoke chronic inflammatory and neuropathic disorders and further to expose their association with several other inflammatory markers through proteomic profiling. In addition, various pharmacological interventions will be scrutinized for efficacy in these chronic hypersensitive models.

e: hoz2@email.uky.edu

Notes:

J Neurol Neurosci, 8:5
DOI: 10.21767/2171-6625-C1-003

Systemic inflammation and neurodegenerative disease

Marcella Reale
University "G. D'Annunzio", Italy

Low-grade inflammatory state is a pathological feature of a wide range of chronic conditions such as neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and multiple sclerosis. The association between inflammation and chronic conditions is widely recognised, and since inflammation inducers may be generated in a disease-specific manner, the issue of causality and the degree to which inflammation contributes and serves as a risk factor for the development of disease is not fully clarified. Communication between the systemic immune system and the central nervous system (CNS) is a critical component of the inflammatory response, and there is evidence for convergence in the mechanisms responsible for the sensing, transduction, and amplification of inflammatory processes that result in the production of neurotoxic mediators. Several studies have suggested that low-grade peripheral systemic inflammation is associated with increased cognitive decline, and that increased risk of developing Alzheimer disease (AD) may be associated with increased systemic inflammation. Increased levels of inflammatory proteins have been found in the brains and plasma samples of patients with dementia. Proinflammatory cytokines, chemokines and prostaglandins promote neuronal death and plus a role in immune to brain communication by activating the central innate immune response, including microglial cells. Recently, the ability of the nervous system to modulate the cytokine production in the immune system was studied; and the so called "cholinergic anti-inflammatory pathway" is responsible of the brain-immune system interface. Knowledge about the cholinergic antiinflammatory pathway as a specific regulator of cytokine responses makes it possible to consider the crosstalk between the CNS and the immune system. Thus, keeping in mind the role of the cholinergic system in inflammation, in addition to the proinflammatory cytokines, the cholinergic agents may be considered as new and interesting therapeutic tools in the pharmacological treatments that may have relevance in neurodegenerative diseases.

e: mreale@unich.it

Notes:

J Neurol Neurosci, 8:5
DOI: 10.21767/2171-6625-C1-003

Potential strategies to improve Temozolomide/radiation therapy of malignant gliomas by targeting glycolytic energy metabolism

Kalyani Thakur[1], Sai Shyam[2] and **Vijay Kumar Kalia[2]**
[1]National Centre for Disease Informatics and Research (ICMR), India
[2]National Institute of Mental Health and Neuro Sciences, India

The current standard treatment of malignant gliomas includes surgery, followed by Temozolomide (TMZ) - Radiotherapy. It leads to increased survival as compared to radiotherapy alone. However, haematological toxicities are also increased by the combination treatments. Therefore, it is important to carry out further preclinical studies, to develop more effective treatment for these tumors. 2-Deoxy-D-Glucose (2-DG), an inhibitor of glycolytic energy metabolism, has been shown earlier to differentially inhibit repair processes, growth and survival of cancer cells. It has been tolerated very well in combination with radiotherapy in clinical trials on malignant gliomas. In the present study, we investigated the effects of combination of clinically relevant concentrations of 2-DG (0.5 mM and 1 mM) and TMZ (2 µM and 5 µM) ± Radiation (1Gy) on cell proliferation, total cellular damage (TCD) and colony formation in an established glioblastoma cell line (U251MG), and primary cultures derived from malignant glioma tumor pieces. The monolayer cultures were grown on cover slips and stained with Acridine Orange (0.002%) after drug treatments and irradiation, for the study of cellular damage and death. Exponentially growing cells were exposed to drugs and Gamma irradiation. Drugs were removed 4 hrs after irradiation and cultures were processed for different assays of cell death and damage. Our results showed that combination of 2-DG with TMZ±Radiation significantly inhibited the cell proliferation up to 6 days. The TCD was significantly increased by the combination of drugs in primary as well as in established cell line. Cell proliferation as measured by MTT assay showed that drugs ± radiation significantly reduced proliferation response. Cell survival inhibition after combination of TMZ+2-DG+Gamma (2µM+0.5mM+1Gy) showed more than additive effects. These results suggest that targeting glycolytic energy metabolism by agents such as 2-DG can enhance the efficacy of TMZ+Radiation Therapy for malignant gliomas, without increasing toxic side effects.

e: kalyani.icmr@gmail.com
kalyani.neuro@gmail.com

Notes:

J Neurol Neurosci, 8:5
DOI: 10.21767/2171-6625-C1-003

The positive clinical consequence of early intervention of combined therapy (omega 3 fatty acids and B12 vitamin) in children under 5 with variable forms of cerebral palsy

Khajik Sirob Yaqob
Zakho General Hospital, Iraq

Background: Cerebral palsy is a common pediatric problem encountered in about 1:3 per 1000 born children and causing variable mental, motor and behavioral dilemmas. Newly introduced trials of neurogenesis with different agents are now extensively evaluated.

Objective: Our study was conducted to evaluate the neurotrophic response to B12 vitamin and omega-3 fatty acids in children diagnosed early with variable forms of cerebral palsy. The response was monitored both clinically and with CT scan as being a highly predictive tool for assessing cerebral palsy.

Design: The study was carried out on 40 cerebral palsy patients; 26 (65%) out of them were girls, and 14 of them were boys, aged from 0 to 5 years old; from outpatient clinic at Zakho/Duhok General Hospital in Kurdistan Region-Iraq. Patients were treated and followed up for 6 months to one year. They were represented and adjusted by full history taking and clinical examination. Brain CT scans were done for every patient to assess the degree of brain atrophy before starting this combined therapy, and every month for six months to one year. There was an improvement in general health of children after interventional therapy.

Results: The study revealed that early intervention of both omega 3 and B12 vitamin in children under 5 with cerebral palsy (CP) shows great response based on clinical examination and CT scan findings. Almost, after combined therapy, 80% of children with delayed speech have very good response and improvement, 77% of children with delayed milestone and hypertonia, and 87% with delayed walking have positive clinical outcomes. Both sexes have equal response to combined therapy. Such findings were obtained as a result of early treatment and diagnosis of children with CP. In addition, among the treated children with CP, improvement in CT scan results was obtained. 84% of treated children have great improvement in their neuroimaging results from moderate/severe forms of brain atrophy to mild form of brain atrophy after being treated and followed up for 6 months - 1 year.

Conclusion: The damaged brain sites based on CT scan results, showed progressive improvement in response to B12 and omega-3 fatty acids upon daily supplement throughout 6 months to one year. However, combining these 2 drugs showed preservative synergistic consequences. B12 vitamin and omega- 3 fatty acids are valuable therapy for children with various forms of cerebral palsy particularly when being linked. The greatest improvement in speech and motor development was significantly observed in about 32 patients (80%) of treated children with B12 vitamin and omega- 3 fatty acids. Others have less response to combined therapy as being presented and diagnosed beyond 1 year of age (16%).

e: khajikyaqob@yahoo.com

Notes:

J Neurol Neurosci, 8:5
DOI: 10.21767/2171-6625-C1-003

Potential of Ocimum sanctum as an adjuvant with sodium valproate in management of epilepsy: An experimental study in rats

Sudhir Chandra Sarangi, Dipesh Joshi, Thomas Kaleekal, Ritesh Kumar and **Yogendra Kumar Gupta**
All India Institute of Medical Sciences, India

For effective control of seizures, antiepileptic drugs (AEDs) are administered at higher dose which is associated with several adverse effects. This study envisages antiepileptic and neuroprotective potential of Tulsi, a commonly used herb for its immunomodulatory property. The optimal dose of Ocimum sanctum hydroalcoholic extract (OSHE) was determined using Maximal Electroshock seizure (MES) and Pentylenetetrazol (PTZ) induced seizure models in Wistar rats (200 to 250g) after administering OSHE (200 – 1000 mg/kg) orally for 14 days. For interaction study, OSHE optimal dose in combination with maximum and submaximal therapeutic doses of valproate was administered for 14 days. Serum levels of valproate were estimated using HPLC for pharmacokinetic study. For pharmacodynamic interaction, antiepileptic effect on above seizure models, neurobehavioral effect using Morris water maze, Passive avoidance and Elevated plus maze tests and antioxidant capacity were assessed. OSHE 1000 mg/kg was found to be optimal providing 50 % protection against both MES and PTZ-induced seizures. Combination of OSHE with valproate did not alter antiepileptic efficacy of valproate significantly. However, the combination showed better memory retention potential in neurobehavioral tests and protection against oxidative stress compared to valproate alone treated groups. Pharmacokinetic parameters did not reveal any significant change in combination group compared to valproate alone. Ocimum, although having per se antiepileptic action, did not affect antiepileptic action of valproate in combination. However, combination treatment has an edge over valproate alone by better neurobehavioral function and reduced oxidative stress, predicting adjuvant potential of Ocimum in epilepsy treatment.

e: scsarangi@gmail.com

Notes:

J Neurol Neurosci, 8:5
DOI: 10.21767/2171-6625-C1-003

The role of the lymphatic system in the development of brain amyloidosis

Miguel Pappolla
St. Michael's Pain and Spine Clinics, USA

Alzheimer's disease (AD) is characterized by brain deposits of a mostly 40 to 42 amino acid peptide, the amyloid β protein (Aβ), in senile plaques and intracranial blood vessels. Aβ exhibits a strong tendency to aggregate into neurotoxic oligomeric forms. The "amyloid hypothesis" of AD proposes that elevated levels of Aβ oligomers trigger a downstream cascade of oxidative and pro-inflammatory events which lead to the widespread death of neurons and dementia. It has been postulated that inadequate clearance of the amyloid β protein (Aβ) plays an important role in the accumulation of Aβ in sporadic late onset AD. While the blood brain barrier (BBB) has taken the center stage in this field, little information is available about the role of the lymphatic system in Aβ clearance. We previously reported that Aβ is cleared through the lymphatic system. We now assessed lymphatic Aβ clearance by treating a mouse model of AD amyloidosis with melatonin, an Aβ aggregation inhibitor and immuno-regulatory neurohormone. We examined Aβ levels in plasma and in lymph nodes of transgenic mice as surrogate markers of vascular and lymphatic clearance, respectively. Treatment with melatonin led to the following changes: 1-A *statistically significant* increase in soluble monomeric Aβ40 and an increasing trend in Aβ42 in *cervical and axillary lymph nodes* of treated mice. 2-*Statistically significant* decreases in oligomeric Aβ40 and Aβ42 in the brain. 3-Lack of changes of Aβ40 and Aβ42 levels in plasma with aging. 4-Elimination of premature mortality in transgenic mice. Several mechanisms involving the lymphatic system in the clearance of cell debris and waste solutes, including amyloid, from the mammalian central nervous system will be discussed. These include lymphatic clearance pathways along cranial nerves, spinal nerves, the cribriform plate, meningeal lymphatic channels and paravascular pathways including the glymphatic system. In addition to the pathways of clearance mentioned here, it is likely that active cellular transport mechanisms are in play. For example, the murine PirB (paired immunoglobulin-like receptor B) and its human ortholog LilrB2 (leukocyte immunoglobulin-like receptor B2), present in human brain, are receptors for Aβ peptides. These receptors, which are members of the immunoglobulin superfamily, are found in dendritic cells. These cells are known to "travel" between brain and lymph nodes. The data that will be presented suggest that abnormalities in the clearance through the lymphatic system may contribute to the development of brain amyloidosis.

e: papppolla@aol.com

Notes: