NEUROSURGERY

P224

CHILDHOOD CAVERNOMAS. A 12-YEAR EXPERIENCE

Monica troncoso, Susana Lara, Daniela Muñoz, Kay Gittermann. Servicio Neurología Infantil Hospital San Borja Arriarán, Universidad de Chie, Santiago Chile.

Introduction: Childhood cavernomas incidence is increasing. His natural history, surgical treatment and clinical outcomes are not well understood in children.

Objective: The aim of this study is to describe the clinical profile of patients with diagnostic of cavernomas in the Pediatric Neurology Department of our Hospital, between 1998-2010.

Methods: N=19 patients. Variables as age, clinical presentation, localization, treatment and evolution were described.

Results: 14 (73, 7%) male, mean age of symptoms debut was 7, 6 years (11 month to 14 years old), 31, 5% of the patients were younger than 3 years and 26, 3% older than ten years.

Clinical manifestations: seizures (63, 2%), focal neurologic signs (31, 6%), cephalalgia (31, 6%). The onset of symptoms were related in 29, 4% with radiological signs of bleeding. 84.2% were solitary lesions located at supratentorial level (73, 7%), brainstem (10, 5%) and spinal cord (10, 5%). Of the supratentorial lesions 64, 3% were left sided and were more frequent in temporal and frontal lobe (both 37, 5%). CT sensibility was 53, 4% and MR 88, 2%. Surgical resection was practiced in 7 cases and no surgical management in 12 cases with favourable results in 4 and 9 cases respectively. Epilepsy was the most frequent complication (21, 5%).

Conclusion: In our group cavernomas were more frequent in men and mostly presented as solitary supratentorial lesions. Epilepsy is the most frequent long term complication, similar to those published in other series.

NEUROTRAUMA

P321

ALTERAÇÕES AUTONÔMICAS EM EMPIEMA PLEURAL SEPTADO: RELATO DE DOIS CASOS PEDIÁTRICOS

Iara Gomes Bittencourt[1], Thaiza Falção[1], Rachel Guimarães[1], Cinthya Varandas[1], Francisco Meneses[1], Aialla Santos[2], Janeusa Leite Primo[1]. [1]Departamento de Neurologia infantil, Obras sociais Irmã Dulce, Brazil; [2]Departamento de Pediatria, Obras sociais Irmã Dulce, Brazil

Alterações autonômicas da síndrome de Claude Bernard Horner (SCBH) apresentam-se quando o impulso nervoso através do nervo simpático responsável pelo suprimento ocular e facial, tem seu trajeto interrompido. Dentre outras causas da síndrome, descrevem-se neoplasias, traumas e fatores iatrogênicos. Relatamos dois casos pediátricos de empiema pleural septado e SCBH, com lesão do plexo braquial em um dos pacientes. Ambos foram abordados cirurgicamente com evolução satisfatória, regressão do quadro infeccioso, melhora da expansão pulmonar e progressiva remissão do quadro neurológico. A síndrome de Claude Bernard Horner secundária, a empiema pleural isolada ou associada a lesão do plexo braquial, embora rara em pacientes pediátricos, pode determinar compressão mecânica da via simpática. Estas alterações são reversíveis quando o diagnóstico e o tratamento adequados são precocemente instituídos.

P322

VESTIBULAR DYSFUNCTION FOLLOWING PAEDIATRIC TRAUMATIC BRAIN INJURY – EXPLORATION OF A NOVEL DIAGNOSTIC TOOL

Karen M. Barlow[1], Alex Scurfield[2], Peter Taeyoung Hong[3], Kathryn Schneider[4], Brian Brooks[5]. [1]University of Calgary; [2]University of Victoria, BC, Canada, Canada; [3]University of Alberta, Canada; [4]Department of Kinesiology, University of Calgary, Canada; [5]Alberta Children's Hospital Research Institue, Canada

Background: It is well established that vestibular injury can occur with traumatic brain injury (TBI). Symptoms that could be related to vestibular dysfunction rather than a brain injury include vertigo, dizziness, and imbalance. Reports indicate that the incidence of dizziness or imbalance secondary to vestibular dysfunction may occur in up to 83% of adults following mild TBI but there are few studies examining this in children. It is difficult, but clinically very relevant, to differentiate symptoms due to vestibular injury as the treatment is very different.

Objective: 1) To examine the symptom of dizziness in children with TBI and 2) Investigate the prevalence of vestibular dysfunction in children following a TBI using a novel diagnostic technique.

Methods: Prospective cohort study. Population: Children aged 11-18 years with a) mild TBI presenting to the Emergency Department (ED) (acute/subacute); and b) mild to severe TBI symptomatic ≥1 month post-injury (chronic). Outcome measures: A new questionaire about dizziness for kids "DizzyKids". Vestibular testing was performed using the Head Impulse test and ICS Impulse goggles, a novel diagnostic tool.

Results: Thirty children (21 males), aged 14.3 (SD+/-2.3) years were enrolled. True "vertiginous" symptoms were not associated with semicircular canal dysfunction. There was a 10% prevalence of vestibular dysfunction in both groups.

Conclusion: Vestibular dysfunction secondary to head trauma occurs in 10% of children with acute mild TBI and in those with chronic post-concussive symptoms. The DizzyKids Questionnaire and ICS Impulse goggles were useful and well tolerated in the pediatric population.

P323

THE FEASIBILITY OF PERFORMING COMPUTERIZED COGNITIVE TESTING AFTER MILD TBI IN A PAEDIATRIC EMERGENCY DEPARTMENT

AneeshKhetani[1], Brian Brooks[2], Karen Maria Barlow[1]. [1]University of Calgary, Canada; [2]Alberta Children's Hospital Research Institute, Canada

Fourteen percent of school-aged children with mild TBI have Post Concussion Syndrome (PCS) for 3 months or longer (Barlow, 2010). Identifying those at risk of prolonged symptoms in the Emergency Department (ED) would be useful. Some studies suggest that computerized cognitive testing (CCT) may help identify these children but it is normally done in the quiet, controlled environment - very different to the busy ED.

Objectives: The aim of this study is to evaluate whether it is feasible to incorporate computerized cognitive testing into the ED management of children with concussion.

Methods: A prospective controlled cohort study. Setting: A busy tertiary referral paediatric ED. Participants: children aged 8-18 years with acute mTBI/concussion and age-matched orthopaedic controls. Feasibility assessment: 30- and 15-minute CCTs were assessed for feasibility using patient and family attitudes, injury variables, medical staff attitudes as well as environmental factors (i.e. space, noise, wait-times etc.).

Results: 74 children aged 12.7 (SD+/-2.2) years (male 54%) with mTBI were enrolled, and 28 orthopaedic controls aged 13 (SD+/-2.4). Impediment factors included noise, testing location, and extra-cranial injuries. Most were mitigated with changes in testing methodology. Participation rates then improved from 27% to 73%. Feasibility data will be presented.

Conclusions: Feasibility data are important when considering CCT in the paediatric ED. Our study, although highlighting the challenges to this novel procedure in an ED setting, suggests that computerized cognitve testing can be performed.

P324

PROTECTIVE EFFECT OF NIUHUANGQINGXIN POWDERS ON EXPERIMENTAL SEIZURE IN DEVELOPING RATS

Xiaolu Chen[1], Wenjuan Li[1], Li Jiang[2]. [1]Ministry of Education Key Laboratory of Child Development and Disorders Key Laboratory of Pediatrics in Chongqing, Chongqing International Science and Technology Cooperation Center for Child Development and Disorders, Chongqing Medical University, China; [2]Department of neurology, children's hospital, Chongqing Medical University, China

OBJECTIVE: To elucidatethe the protective effect of a Chinese herb Niuhuang Qingxin Powders(NQP) on experimental seizure induced by Pentetrazol.

MATERIALS AND METHOD: 32 Sprague-Dawley rats aged 21 days were randomly divided into 4 groups: saline control group, diazepam group(2.632 mg/kg), three incremental doses of NQP groups including low-(0.3 g/kg), moderate-(4 g/kg) and high dosage-(8 g/kg). Half an hour after administration of saline, diazepam and NQP by gavage, the seizure was produced by intraperitoneal injection of pentetrazol(70 mg/kg). Then onset latency, duration and level of seizure of each rat were assessed, and an in vivo EEG recording was conducted.

RESULTS: Compared with saline control, administration of high-dose NQP significantly increased length of seizure latency(p=0.021). Low and moderate dosage NQP failed to show a significant difference in seizure latency compared with saline control(p=0.721, 0.547 respectively). Compared with saline control, administration of three doses of NQP decreased seizure duration significantly (p<0.05). Moderate, high-dosage NQP decreased seizure duration even more significantly compared with low dosage NQP(p=0.001, p<0.001 respectively). Moreover, administration of high-dose NQP decreased the average seizure level compared with saline control (p=0.02), while low and moderate dosage NSP groups failed to decrease the seizure level significantly compared with saline control (p=0.105, p=0.234 respectively). EEG recording showed that spike amplitudes and spike frequencies in high dosage NQP group rats were significantly lower than rats in saline control, the low, and the moderate dosage NQP groups.

CONCLUSION: High-dose NQP exhibits a protective function on rats with pentetrazol induced seizure.

P325

PROTECTIVE EFFECT OF NIUHUANGQINGXIN POWDERS ON HYPERTHERMIA INDUCED SEIZURE IN DEVELOPING RATS

Xiaolu Chen[1], Wenjuan Li[1], Hengsheng Chen[1], Li Jiang[2]. [1]Ministry of Education Key Laboratory of Child Development and Disorders, Key Laboratory of Pediatrics in Chongqing, Chongqing International Science and Technology Cooperation Center for Child Development and Disorders, Chongqing Medical University, China; [2]Department of neurology, children's hospital, Chongqing Medical University, China

OBJECTIVE: To investigate the effect of NiuhuangQingxin Powders (NQP) on convulsive behavior induced by hyperthermia in prepubertal rats.

MATERIALS AND METHOD: 32 Sprague-Dawley rats were assigned to 4 groups (n=8), saline control, diazepam group(2.632 mg/kg), three incremental doses of NQP groups including low-(0.3 g/kg), moderate-(4 g/kg) and high dosage-(8 g/kg). Half an hour after administration of saline, diazepam and NQP by gavage, rats were placed in a glass container, and hyperthermia was induced by using a regulated stream of hot water (45°C). Then onset latency, duration and level of hyperthermia induced seizure of each rat were assessed.

RESULTS: Compared with saline control, administration of diazepam and all three doses of NQP significantly increased length of seizure latency (p<0.05). And administration of diazepam and high doses of NQP also decreased seizure duration significantly compared with saline control (p<0.05), while low and moderate dosage NQP groups failed to decrease seizure duration significantly. Moreover, administration of diazepam and high-dose NQP decreased the average seizure level compared with saline control (p<0.05), while low and moderate dosage NQP groups failed to decrease the seizure level significantly.

CONCLUSION: High-dose NQP exhibits a protective function on rats with hyperthermia induced seizure.

P326

PREDICTORS OF OUTCOME IN NON-TRAUMATIC COMA IN A PEDIATRIC COHORT FROM SOUTH INDIA: RESULTS OF A MULTIVARIATE ANALYSIS.

Vykuntaraju K Gowda, Ningappa B Bannigidad, Praveen-kumar Srikanteswara, Govindraj M, Premalatha R. Indira Gandhi Institute of Child Health, Bangalore, India.

Objective: To study the etiology and clinical profile of non-traumatic coma in children and to determine the predictors of outcome

Methods: one hundred and four consecutive children between 2mo – 12 yr were studied. The clinical signs at admission: vital signs, Glasgow coma scale, respiratory pattern, papillary reflex, extraocular movements, fundus picture and motor deficits were recorded. Etiology of coma was determined by clinical history, examination and relevant investigations. Their progress was monitored clinically, biochemically and with multisystem monitors. Outcome was recorded as survived or died. Chi-square and Fisher exact test were used to test the significance of study parameters. Multivariate logistic regression was used to find the predictors for outcome.

Results: Etiology of coma was intracranial infections in 65%, metabolic in 20% and others. Sixteen percent had residual neurodeficits, 16% died. Survival was better in children with intracranial infections (13%) as compared to metabolic coma (33%). On multivariate logistic regression, bradycardia, hypotension, abnormal respiratory pattern, duration of coma > 48 hrs, GCS < 7 at admission, unequal & non-reactive pupils, papilledema, abnormal extraocular movements, motor deficits, signs of meningitis correlated with mortality. Requirement of ventilatory support and abnormal CT findings correlated with mortality.

Conclusion: Intracranial infections were the most common cause; the most common cause of death being metabolic coma. Simple clinical signs and relevant investigations served as prognostic indicators of outcome.

P327

A STUDY TO EVALUATE THE ETIOLOGICAL PROFILE OF ACUTE ENCEPHALITIC SYNDROME

Sitaraman Sadasivan, Ishu Goyal. S.M.S.Medicalcollege,Jaipur, India

OBJECTIVE: To study the etiological profile of acute encephalitic syndrome with special reference to infectious etiology.

METHODS: It is an observational study done in department of pediatric medicine, SMS medical college, Jaipur from April 2012 to April 2013. The sample size of 260 was calculated with inclusion criteria – 1) age: 3 months to 18 years. 2) fever: (>38°c) of duration <15 days. 3) altered sensorium >24 hrs (Glasgow Coma Score <12). Exclusion criteria - head injury, simple febrile seizures, seizure disorder, heat stroke, metabolic disorders.

RESULTS: The final study group comprised of 330 patients with male: female ratio of 1.64: 1. CNS Tuberculosis was the most frequent diagnosis 83 (25.1%) followed by viral encephalitis 73 (22.1%), and cerebral malaria 45 (13.6%). The most common etiological agent identified in viral encephalitis group was herpes simplex in 27 patients (8.1%). The other viruses identified were dengue virus 17 (5.1%), varicella (2.4%), measles (2.4%) and Japanese encephalitis (2.4%). Other causes were hepatic encephalopathy (7.5%), enteric encephalopathy (4.5%) and scrub typhus (3.9%).

Out of 330 cases of acute febrile encephalopathy, the case fatality rate was 13% and 20 (6%) patients had significant neurological sequels at discharge. Maximum number of cases were recorded in September - 91(27.5%).

CONCLUSIONS: The infectious etiology of acute encephalitic syndrome varies from tubercular to viral, pyogenic, rickettesial to parasitic. The cases were almost evenly distributed throughout the year, with an upsurge towards the end of monsoon season.

P328

THE TYMPANIC MEMBRANE DISPLACEMENT ANALYSER FOR MONITORING INTRACRANIAL PRESSURE IN CHILDHOOD ACUTE COMA

Samson Awili Gwer.Neurophysiology Unit, Medical physiology, College of Health Sciences, Kenyatta University, Kenya

Background: We investigated the utility of Tympanic Membrane Displacement (TMD) Analyser in monitoring children with acute coma

Methods: Between November 2007 and September 2009, we made serial TMD and clinical observations on children with acute coma (Blantyre coma score ≤ 2) at the paediatric high dependency unit of our hospital. We examined middle ear function using tympanometry and measured cardiac pulse (CPA) and respiratory pulse pressure amplitudes (RPA) using the TMD analyser. We applied multivariable logistic regression to examine the association between TMD measurements and, clinical features of raised ICP, and death.

Results: We recruited 75 children [median age 3.3 (Inter-quartile range (IQR) 2.0, 4.3) years].Children with clinical features of raised ICP had higher maximum CPA [median 248 (IQR 198,350) nl] and RPA [median 487 (IQR 295,836) nl] measurements in the semi-recumbent position compared to those without; [CPA median 158 (IQR 123,288) nl; P=0.02, and RPA median 292 (IQR 183,365) nl P<0.01]. A unit rise in log of initial semi-recumbent CPA and RPA, and recumbent CPA measurements, were associated with increased risk of death; Odds ratio (OR) 4.0 (95%C.I. 1.3, 12.3; P=0.01), OR 3.7(95%C.I. 1.0, 14.1; P=0.05) and OR 3.5(95%C.I. 1.3, 9.3; P=0.01) respectively. Abnormal tympanometry was associated with greater risk of death compared to normal tympanometry (OR 16.3 95% C.I. 1.7-158.5; P<0.01).

Conclusion: TMD pulse pressure measurements predict death and may be useful in detecting and monitoring raised ICP in childhood coma. Abnormal tympanometry appears to predict death and may be related to altered ICP dynamics.

P329

NEUROPROTECTIVE EFFECT OF MILD HYPOXIA IN ORGANOTYPIC HIPPOCAMPAL SLICE CULTURES OF RAT

Soo Ahn Chae[1], Na Mi Lee[2], Seh Hyun Kim[2], Woo Soon Lee[2]. [1]College of Medicine Chung-Ang University/Chung-Ang University Hospital, South Korea; [2]Chung-Ang University Hospital, South Korea

Purpose: Hypoxia is known to cause brain damage. However, we think there may be the difference of the effect on the brain according to the degree of hypoxia. The aim of this study is to investigate the potential effect of mild hypoxia.

Methods: We used hippocampal tissue cultures at 7 and 14 days in vitro (DIV) from SD rats aged 7 days. The tissue cultures were exposed to 10% oxygen for 60 minutes. 24 hours after this hypoxic insult, propidium iodide fluorescent images were obtained. Damaged areas in CA1, CA3, and DG were measured using image analysis software. We estimated the extent of damage 24 hours after hypoxic exposure. Hypoxia exposed tissues were compared to tissues not exposed to hypoxia. The ratio of damaged area at 24 hours to the total damaged area after NMDA treatment was calculated.

Results: In the 7 DIV group, compared to control tissues, hypoxia-exposed tissues tended to have decreased damage in two regions (CA1, DG), but this decrease was not statistically significant. In the 14 DIV group, compared to control tissues, hypoxia-exposed tissues showed decreased damage; this decrease was not significant in the CA3 and, DG, but it was significant in the CA1.

Conclusion: Most tissues showed a tendency to have less damage after hypoxic exposure. Therefore, we think that mild hypoxia might have a protective effect in the brain.

P330

PROTECTIVE EFFECTS OF NOVEL ANTIEPILEPTIC DRUG LACOSAMIDE IN EXPERIMENTALLY INDUCED TRANSIENT CEREBRAL ISCHEMIA

Sung Koo Kim[1], Bing Chun Yan[2], Joon Ha Park[2], Moo-Ho Won[2]. [1]Hallym University Dontan Sacred Heart Hospital, South Korea; [2]School of Medicine, Kangwon National University, South Korea

Lacosamide, a novel antiepileptic drug, has been discovered to have some beneficial effects beyond its effectiveness. In the present study, we examined the neuroprotective effect of lacosamide against ischemic damage in the hippocampal CA1 region following 5 min of transient cerebral ischemia in gerbils. The results showed that pre- and post-treatment with 25 mg/kg lacosamide protected significantly neuronal death from transient cerebral ischemic injury. Many CVpositive cells, NeuN-immunoreactive neurons and a few number of F-J B-positive cells were found in the stratum pyramidale of the CA1 region in the lacosamide-treated ischemia-operated groups compared with those in the vehicle-treated ischemia-operated group. In addition, treatment with lacosamide also markedly attenuated the activation of astrocytes and microglia in the ischemic CA1 region. On the other hand, we examined that treatment with lacosamide increased and maintained the antioxidants levels; and TNF-α and BDNF immunoreactivities were increased significantly after lacosamide treatment following transient cerebral ischemia. In brief, these results indicate that both pre- and post-treatment with lacosamide can protect CA1 pyramidal neurons from transient cerebral ischemic injury in the hippocampus, and the neuroprotective effect of risperidone may be related to the maintenance of antioxidants as well as the increase of TNF-α and BDNF levels.

P331

CLINICAL FEATURES OF ENCEPHALOPATHY IN CHILDREN WITH BURNS

Olga Lvova[1], Olga Kovtun[1], Anna Orlova[2], Elena Orlova[2], FedorBrezgin[1], Aleksey Shtukaturov[2]. [1]Ural State Medical University (USMU), Russian Federation; [2]City Children's Clinical Hospital №9, Russian Federation

INTRODUCTION: Clinical features of burn encephalopathy in children are not investigated thoroughly.

METHODS: Type of study: case series, 44 patients. Inclusion criteria: boys (n=25) or girls (n=19) between the age of 7 month and 13 y.o. with neurological signs, which developed during 0-7 days after burn trauma have occurred.

RESULTS: The average age was 2,9y.o., the average square of burned area was 28% (varied from 10% to 80%), 19 (43, 2%) had II, 16 (36, 4%) had III grade of severity. The majority of patients were admitted from countryside 35 (75%), 25 (56, 8%) had HIE in their perinatal history. All children were admitted to ICU, were taken on ALV (n=11, 25% on average 9, 5 days), took more than 2 operations and were treated for burn shock in 36 (81, 8%) and SIRS in 33 (70, 5%) cases. In the burns unit patients required wound dressing under the intravenous anesthesia (3,4±1,2 times on 25-45 minutes), had fresh frozen plasma and blood components' transfusions in 35 (75,0%) cases. We identified brisk of tendon jerks 24 (54, 5%), muscular hypotonia 7 (15, 9%), tremor 10 (22, 7%), nystagmus 7 (15, 9%), seizures 3 (6, 8%) in neurological assessment in those children.

CONCLUSION: So called **b**urn encephalopathy in children stays a comprehensive issue, apparently depends on the square and severity of burn trauma as well as premorbid and social status. We consider the combination of iatrogenic factors to play the great role in this problem, such as the quality of urgent care, quantity of intravenous anaesthesia, antibiotics and so on.

P332

ZONISAMIDE ATTENUATES HYPEROXIA-INDUCED APOPTOSIS IN THE DEVELOPING RAT BRAIN

Yasemin Topcu. Dokuzeylul University Medical School, Turkey.

Aim: Oxygen therapy used in the treatment of perinatal hypoxia induceneurodegeneration in babies with immature antioxidant mechanisms. Zonisamide is a new antiepileptic drug used in childhood intractable seizures. Many studies demonstrated its neurprotective effects. There is no study evaluating its effect on hyperoxic brain ınjury. The aim of this study is to investigate the neuroprotective effect of zonisamide on hyperoxia induced neonatal brain injury.

Material and Methods: A total of 21 Wistar rat pups were used. The animals were divided into three groups: control group, hyperoxia group, and zonisamide-treated group. Wistar rat pups in the hyperoxic groups were exposed to 80% oxygen from birth until postnatal day 5. The hyperoxia + zonisamide group received an intraperitoneal injection of zonisamide. We used TUNEL and active Caspase-3 examination to demonstrate cell death and apoptosis in hippocampus, prefrontal and parietal cortex of neonatal rats which were exposed to hyperoxia.

Results: The number of neurons in hippocampus, prefrontal and parietal cortex significantly decreased in hyperoxia group compared to control group. Zonisamide significantly preserved the number of neurons in CA1 and dentate gyrus parts of hippocampus, prefrontal and parietal cortex. Zonisamide treatment also decreased the number of apototic neurons in all examined parts of hippocampus, prefrontal and parietal cortex.

Conclusion: We suggest that zonisamide treatment may be used as a neuroprotective agent in hyperoxic brain injury.

P333

A NOVEL METHOD OF EXPERIMENTAL TRAUMATIC BRAIN INJURY IN RODENTS: VALIDATION STUDY

Hameed BA[1,2], Brown P[3], Lolait S[1], Carroll A[1], Lightman SL[1], Sharples PM[1]. [1]Henry Wellcome Laboratory for Integrated Neuroscience and Endocrinology, University of Bristol; [2]Department of Paediatric Neurology, Bristol Royal Hospital for Children; [3]Department of Medical Physics, Frenchay Hospital, Bristol, UK.

Objective: Lateral fluid percussion injury model (LFPI) is widely used in experimental traumatic brain injury (TBI) research, particularly in rats. In the classical model, a pendulum strikes a fluid-filled system connected to the dura, producing acceleration-deceleration TBI. Accurate pendulum levelling is difficult, adversely affecting reproducibility, and the equipment bulky and expensive. To overcome these shortcomings, we have developed and validated a micro-FPI apparatus modelled on a novel system1.

Methods: Our micro-FPI apparatus consists of a Picospritzer II TM (Parker Hannifin, Pneutronics Division, PineBrook, NJ) device that uses a high-speed valve to deliver a standardized pressure pulse of air to a standing column of fluid. Pressure pulses are triggered manually or electronically. Physiological response to injury was assessed by mortality; duration of suppression of somatomotor reflexes; and arterial blood pressure changes monitored invasively via a femoral artery cannula.

Conclusion: Our micro-FPI device produces a LFPI similar to that described by researchers using classical LFPI. Our pathophysiological data suggests that micro-FPI 40psi delivered over 20milliseconds produces moderate severity TBI.

P334

SPIRONOLACTONE, BUT NOT MIFEPRISTONE, ENHANCES UPREGULATION OF BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF) AND NEUROTROPHICTRK B RECEPTOR (TRK B) GENE EXPRESSION IN A RAT MODEL OF TRAUMATIC BRAIN INJURY (TBI)

Hameed BA[1,2], Brown P[3], Lolait S[1], Carroll A[1], Lightman SL[1], Sharples PM[1]. [1]Henry Wellcome Laboratory for Integrated Neuroscience and Endocrinology, University of Bristol; [2]Department of Paediatric Neurology, Bristol Royal Hospital for Children; [3]Department of Medical Physics, Frenchay Hospital, Bristol, UK.

Objective: TBI is a major cause of acquired disability in children.. The commonest sequel is cognitive dysfunction, resulting from selective hippocampal damage. Glucocorticoids and mineralocorticoids are steroid hormones which act through specific receptors (GR and MR), playing a critical role in hippocampal neuronal survival and plasiticity. Neurotrophins may mediate the actions of glucocorticoids on neuronal survival. The study aim was to investigate the impact of therapeutic modulation of GR/MR balance on the neurotrophic response to TBI, using an experimental model..

Methods: Adult male Wistar rats were subjected to moderate fluid percussion injury (FPI) or sham-injury under full general anaesthesia. One hour pre-surgery, subjects were administered control vehicle; GR-blocker (mifepristone) or MR-blocker (spironolactone). Animals were sacrificed six hours post-surgery. In situ hybridisation studies were performed, using radiolabelled oligoprobes to mRNA for Brain Derived Neurotrophic Factor (BDNF) and its tyrosine receptor (Trk-B). ANOVA compared optical density measurements for BDNF and Trk-B mRNA between six groups: 1) sham-injury/vehicle; 2) FPI/vehicle; 3) sham-injury/ spironolactone; 4) FPI/spironolactone; 5) sham-injury/ mifepristone; 6) FPI/mifepristone.

Results: Significant group differences were seen for BDNF and Trk B mRNA expression in all hippocampal regions (DG, CA1, CA2, CA3), both ipsilateral and contralateral to injury (all, $p<0.0001$). Post-hoc analysis demonstrated significant differences between sham- injured and FPI rats and between FPI spironolactone rats and FPI mifepristone or vehicle rats for BDNF mRNA (e.g. ipsliateral CA1, FPI/mifepristone vs. FPI/spironolactone $p=0.002$; CA2, FPI/vehicle vs. FPI/spironolactone $p<0.0001$; CA3, FPI/vehicle vs. FPI/spirolactone $p<0.0001$, FPI/ mifepristone vs. FPI spironolactone $p=0.001$) and Trk-B mRNA (e.g. DG, FPI/mifepristone vs. FPI spironolactone $p=0.001$; CA2, FPI/vehicle vs. FPI/spironolactone $p<0.0001$; CA3, FPI/vehicle vs. FPI/spironolactone $p<0.0001$, FPI/mifepristone vs. FPI/ spironolactone $p=0.017$). Pre-injury spironolactone enhanced TBI-induced up-regulation of BDNF and Trk-B mRNA.

Conclusions: Selective blockade of MRs by spironolactone enhances the neurotrophic response to experimental TBI. Further research will explore the impact on histological and cognitive outcome.

P335

FATAL OUTCOME FOLLOWING FIRST INFLIXIMAB INFUSION IN A CHILD WITH INFLAMMATORY BOWEL DISEASE

Fiona Mitchell Baumer, Niyati Mehta, Paul Rufo, Jodie Ouahed, Jay Thiagarajah, Menno Verhave, Michael Rivkin. Boston Children's Hospital, United States

Introduction: Infliximab is a monoclonal antibody against TNF-α used in the treatment of various autoimmune diseases, including rheumatoid arthritis and inflammatory bowel disease. Previously reported neurologic complications in children include central and peripheral demyelinating disorders and neuropathies that usually occur months after initiation of therapy.

Case Description: A 7 year old male with a diagnosis of ulcerative colitis and primary sclerosing cholangitis received an infusion of infliximab after failing outpatient oral medications. He tolerated the infusion well but six hours later awoke with headache and emesis, rapidly became obtunded, and required intubation. His exam was notable for minimally reactive pupils and loss of all other brainstem reflexes. Cranial CT found hypodense lesions in the bilateral cerebral hemispheres, cerebellum and pons accompanied by hemorrhage. MRI showed diffusion restriction concerning for ischemic infarcts. On careful review, areas of ring-enhancement suggestive of either inflammation or blood-brain barrier degradation were found. MRA and MRV were unremarkable. Labs were notable for an extremely elevated d-dimer. CSF was grossly bloody but otherwise bland. Infectious studies were negative. Echocardiogram showed depressed ventricular dysfunction but neither intracardiac shunt nor thrombus were seen. Intracranial pressure was monitored and hyperosmotic therapy was administered. Malignant intracranial hypertension did not develop. Within three days, he lost all brainstrem reflexes and was terminally extubated. Autopsy was refused.

Discussion: This case is relevant to the neurologic community as it is the first to suggest that infliximab can cause fulminant, fatal CNS consequences even after the initial dose.