Session 01: Dementia and Neurorehabilitation
Background: Dysphagia is a common complication following cerebrovascular disease, causing significant disability due to increased risk of malnutrition and pneumonia. Repetitive transcranial magnetic stimulation (rTMS) is a viable non-invasive therapeutic agent that has been seen in RCTs to have possible benefits in swallowing rehabilitation.

Objective: To evaluate the superiority of real rTMS versus sham rTMS in treating post-stroke dysphagia.

Methodology: Several online databases were searched from their earliest record to 31 July 2015 for RCTs that used repetitive transcranial magnetic stimulation to treat post-stroke dysphagia. The Jadad scale was used to assess the quality of the included studies. The weighted mean difference (WMD) between baseline and post-treatment mean for Penetration Aspiration Scores (PAS) measured in the experimental and control groups were extracted for subsequent meta-analyses.

Results: Seven studies were identified, three of which used the PAS and were analyzed. There was a significant weighted mean difference (WMD) in PAS score using liquid bolus two weeks after treatment in two good quality studies, \(-1.14 (95\% \text{ confidence interval (CI)} = -1.80 - -0.48, P = 0.001)\) without significant heterogeneity \(I^2 = 0.0\%), as well as a significant decrease of PAS between real and sham/wrong site rTMS after four weeks, \(-1.83 (CI = -3.22 - -0.44, P = 0.010)\) also without significant heterogeneity \(I^2 = 0.0\%).

Conclusion: Treatment of post-stroke dysphagia with rTMS translated to improved scores on one functional outcome rating for aspiration on subgroup analyses in studies using liquid bolus after two weeks, and between real and sham treatment after four weeks.
A COMPARATIVE STUDY OF DUOXETINE AND PAROXETINE IN JAPANESE PATIENTS WITH POST-STROKE DEPRESSION

S. Matsumoto

Kagoshima University, Department of Rehabilitation and Physical Medicine, Kirishima City, Japan

Introduction/Background

Duloxetine is an anti-depressant that inhibits the reuptake of serotonin and norepinephrine. We considered that it is important to verify the anti-depressant effect of duloxetine.

Material and Methods

A double-blind, parallel-group, controlled study was performed to investigate if duloxetine was superior to paroxetine in terms of improvement in symptoms of depression and pain in Japanese patients with post-stroke depression in a fixed-dose design. The efficacy and safety of duloxetine 60 mg/day were also assessed in comparison with those at the standard dose of 40 mg/day.

Results:

Changes in 17-item Hamilton depression rating scale (HAM-D) total score (mean ± standard deviation) for group D1 (duloxetine 40 mg/day), group D2 (duloxetine 60 mg/day), and group PX (paroxetine 20 mg/day) were −14.9 ± 5.6, −15.6 ± 6.4, and −11.4 ± 6.2, respectively, and the estimated differences in total score for group PX were 3.8 for group D1 and 4.2 for group D2. The superiority of groups D1 and D2 to group PX was thus confirmed, because the upper confidence limit of differences between groups D1 and PX and between groups D2 and PX was more than 3.2. The groups D1 and D2 presented a reduction in the pain, which was not observed in the group PX. The incidence of treatment-related adverse events was 21% for group D1, 28% for group D2, and 30% for group PX, indicating no significant difference between the three groups.

Conclusion:

These results demonstrate that duloxetine 40 mg/day and 60 mg/day is superior to paroxetine in terms of efficacy on post-stroke depression and central pain.
This study was done to demonstrate the effects of Ephedrine HCL, Turmerone & Curcumin in Neurogenesis and Inhibition of Beta Amyloids in Transgenic Mice. The transgenic mice models used contain mutations associated with familial Alzheimer's disease (APP Swedish, MAPT P301L, and PSEN1 M146V). These mice develop age-related, progressive neuropathology including plaques and tangles. Ten-month-old male and female APPSw Tg+ and Tg− mice from 12 litters were randomly split between treatment groups. Tg+ mice were fed either chow containing a low dose of curcumin (160 ppm; n=9; a high dose of curcumin (5000 ppm; n=6), or no drug (n=8) for 6 months. Mice with low and high dose of curcumin were given specific doses of 0.02% Ephedrine HCL injection every 72 hours and underwent a single intracerebroventricular injection of 3mg ar-turmerone. To evaluate whether curcumin treatment affected plaque pathology, cryostat hemibrain sections from Tg+ control and Tg+ low-dose curcumin-treated mice were immunostained with an antibody against Aβ1−13 (DAE). Two-factor ANOVA revealed a significant reduction in plaque burden in curcumin, Ephedrine HCL and turmerone treated animals (F (1,60) = 4.74; p=0.03), in which amyloid burden was decreased by 43.6% in treated animals compared with untreated animals. Soluble Aβ in Tg+ untreated and Tg+ low-dose curcumin mice were measured by sandwich ELISA. Two-way ANOVA showed significant treatment effects in decreasing the levels of soluble Aβ (*p < 0.05). Underlying mechanistic pathways that might link curcumin treatment to increased cognition and neurogenesis via exon array analysis of cortical and hippocampal mRNA transcription showed a positive result.
ASSOCIATION OF FRONTOTEMPORAL DEMENTIA GWAS LOCI WITH LATE-ONSET ALZHEIMER’S DISEASE IN A NORTHERN HAN CHINESE POPULATION

C.C. Tan1, J.T. Yu1, L. Tan1
1QingDao Municipal Hospital East, Neurology, QingDao, China

Background: Both Alzheimer’s disease (AD) and frontotemporal dementia (FTD) are a class of neurodegenerative diseases. Strong similarities in cerebrospinal fluid biomarker, imaging markers, and disease progression profiles suggest that some or most of the pathophysiology is shared between AD and FTD. A recent large genome-wide association study reported several single nucleotide polymorphisms (SNPs) at the RAB38, RAB38/CTSC, HLA-DRA/HLA-DRB5, and BTNL2 in association with FTD. Objective: To explore whether these SNPs are associated with AD risk. Methods: We conducted a case-control study to investigate the association of FTD-associated loci in 2338 Han Chinese subjects. Results: We observed significant differences in genotype distributions of rs302668 (pc = 0.025), rs9268877 (pc = 0.025), rs9268856 (p < 0.001), and rs1980493 (pc = 0.045) between cases and controls. The SNP rs16913634 for RAB38/CTSC was unrelated to LOAD risk (p = 0.088). Conclusion: The SNPs rs302668 in RAB38, rs9268877 and rs9268856 polymorphism in HLA-DRA/HLA-DRB5, and rs1980493 polymorphism in BTNL2 might play a role in the susceptibility to late-onset AD in the Han Chinese population.
DIFFERENTIAL EFFECTS OF APOE GENOTYPES ON THE ANTERIOR AND POSTERIOR SUB-NETWORKS OF DEFAULT MODE NETWORK IN AMNESTIC MILD COGNITIVE IMPAIRMENT

B. Yuan¹, Z. Zhang¹, J. Chen¹
¹ZhongDa Hospital- Medical School- Southeast University, Department of neurology, Nanjing, China

Background. The APOE gene is considered as the major genetic susceptibility factor for Alzheimer's disease. Recent studies have suggested that the default mode network (DMN), based in ventromedial prefrontal cortex (vmPFC) and posterior cingulate cortex (PCC), consists of functionally differentiable anterior and posterior subnetworks. Our study was to investigate whether there are differential effects of APOE polymorphism on DMN subnetworks in aMCI.

Method. We used a seed correlation approach to perform functional connectivity (FC) analyses in DMN subnetworks in 74 aMCI and 105 healthy controls. The logistic regression analysis was performed to obtain a model for classifying aMCI and HC subjects.

Results. Significant interactions of APOE genotype by aMCI on FCs were found in several brain regions in vmPFC subnetwork and PCC subnetwork. The impairment of episodic memory (EM) for ε4-carriers in aMCI negatively correlated with the altered FC between vmPFC and right middle cingulate cortex (MCC) while positively correlated with the altered FC between PCC and left fusiform gyrus (FG). The regression analyses demonstrated that a model composed of EM, FC between vmPFC and right MCC, and FC between PCC and left FG, dexterity correctly classified 89.4% of the aMCI and HC subjects.

Conclusions. These results provide a novel insight that APOE ε4 and ε2 alleles differentially mediate the anterior and posterior DMN subnetworks, which ε2-carriers in aMCI play a protective role in contributing to a compensatory mechanism in anterior DMN subnetwork. Furthermore, the anterior and posterior DMN subnetworks in aMCI play an opposing role on the impairment of EM.
Session 02: Movement Disorder + Neurosciences (Current status in Stem Cell Therapy) + Headache and Pain
LINK BETWEEN WILLIS-EBMOM DISEASE AND MIGRAINE WITH AURA

B.A. Acar¹, T. Acar², A.N. ALAGOZ¹

¹Sakarya University Faculty of Medicine, Department of Neurology, SAKARYA, Turkey
²Sakarya University Education and Research Hospital, Department of Neurology, SAKARYA, Turkey

Abstract: Background and purpose: We have investigated the prevalence and characteristics of definite migraine in patients with primary Willis-Ekbom Disease (WED) (primary Restless Legs Syndrome; pRLS) and matched controls.

Methods: We evaluated 63 consecutive adult pRLS patients as well as 141 age- and sex-matched controls in a case-control study. The diagnosis of migraine and the subtypes was defined by the "International Classification of Headache Disorders-II" (ICHD-II). Only "definite" migraineurs were included to the study.

Results: The mean age of 63 adult pRLS patients (15 men, 48 women) participated in the study was 49.4. A total of 27 patients (42.9 %) had definite migraine. Of these migraineurs, 7 (11.1 %) were without aura and 20 (31.8 %) were with aura. The mean age of the 141 control subjects was 48.7. A total of 32 patients (22.7 %) did experience migraine, and of these migraineurs 28 (19.9 %) were without aura and 4 (2.8 %) were with aura. Migraine and migraine with aura were significantly more common in pRLS patients than the control group (Table 1).

Conclusions: pRLS patients showed a positive association with definite migraine headaches. In contrast to results highlighted in recent studies, we found a strong link between migraine with aura and pRLS.
Disclosure: The authors declare that there are no conflicts of interests.

Table 1. Demographic, clinical features and the prevalence of migraine of the study sample

<table>
<thead>
<tr>
<th></th>
<th>Control (n=141)</th>
<th>pRLS (n=63)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Sexuality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>31.2%</td>
<td>44</td>
<td>23.8%</td>
</tr>
<tr>
<td>Female</td>
<td>68.8%</td>
<td>97</td>
<td>76.2%</td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.7±8.1</td>
<td></td>
<td>49.4±11.7</td>
</tr>
<tr>
<td>Beck-D (score)</td>
<td>8.4±6.8</td>
<td></td>
<td>16.0±9.1</td>
</tr>
<tr>
<td>Beck-A (score)</td>
<td>11.9±11.5</td>
<td></td>
<td>21.6±12.9</td>
</tr>
<tr>
<td>PSQI (score)</td>
<td>5.2±3.1</td>
<td></td>
<td>10.9±3.9</td>
</tr>
<tr>
<td>Migraine (+)</td>
<td>22.7%</td>
<td>32</td>
<td>42.9%</td>
</tr>
<tr>
<td>M-Aura (+)</td>
<td>2.8%</td>
<td>4</td>
<td>31.8%</td>
</tr>
<tr>
<td>M-Aura (-)</td>
<td>19.9%</td>
<td>28</td>
<td>11.1%</td>
</tr>
</tbody>
</table>

pRLS (primary Restless Legs Syndrome), Beck-D (Beck Depression Inventory), Beck-A (Beck Anxiety Inventory), PSQI (Pittsburgh Sleep Quality Index), M-Aura (Migraine with Aura)
Objective: Restless legs syndrome (RLS) is characterized by abnormal sensations in the extremities, especially in the legs, as well as dysesthesia. The etiology of RLS has not been determined until recently. RLS may be associated with systemic inflammation. The neutrophil to lymphocyte ratio (NLR) is a new and simple marker indicating systemic inflammation. The aim of the present study was to investigate the relationship between systemic inflammation and RLS through the use of NLR.

Methods: A total of 75 newly diagnosed patients with RLS (Group1) and 56 healthy control subjects (Group2) were included in this study. Baseline NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. NLR levels were compared between the two groups.

Results: There were no significant differences in sex and age between the two groups. NLR was 1.96±0.66 in the patient group and 1.67±0.68 in control group (p=0.005) (Table1-2) NLR was predictive at 1.58 with a 64% sensitivity and 50% specificity for RLS (Figure-1). NLR levels were found to be statistically higher in patients with RLS.

Conclusion: The etiology of RLS remains undetermined. Our study shows that systemic inflammation may play a role in RLS. It may also be that RLS is related to systemic inflammatory diseases. High NLR values supports this relationship.
Table 1: Demographic Characteristics

<table>
<thead>
<tr>
<th>Parameters</th>
<th>RLS</th>
<th>Control</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>75</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Male/Female (n)</td>
<td>16/59</td>
<td>19/37</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>45.6±9.4</td>
<td>48.09±11.4</td>
<td>0.184</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.9±5.9</td>
<td>28.3±5.3</td>
<td>0.499</td>
</tr>
</tbody>
</table>

*RLS: Restless Legs Syndrome

Table 2: Hematological parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>RLS (n:75) Mean ±SD</th>
<th>Control (n:56) Mean ±SD</th>
<th>Normal Range</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>13.1±1.4</td>
<td>13.4±2.1</td>
<td>12.2-18.1</td>
<td>0.28</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>38.7±4.0</td>
<td>39.4±5.6</td>
<td>37.7-53.7</td>
<td>0.5</td>
</tr>
<tr>
<td>WBC (K/ul)</td>
<td>6.8±1.6</td>
<td>6.3±2.0</td>
<td>4.6-10.2</td>
<td>0.69</td>
</tr>
<tr>
<td>Neutrophil (K/ul)</td>
<td>4.0±1.2</td>
<td>3.4±1.3</td>
<td>2.0-6.9</td>
<td>0.69</td>
</tr>
<tr>
<td>Lymphocyte (K/ul)</td>
<td>2.1±0.6</td>
<td>2.2±0.8</td>
<td>0.6-3.4</td>
<td>0.85</td>
</tr>
<tr>
<td>Platelet (K/ul)</td>
<td>292±78</td>
<td>284±64</td>
<td>142-424</td>
<td>0.71</td>
</tr>
<tr>
<td>NLR</td>
<td>1.96±0.66</td>
<td>1.67±0.68</td>
<td></td>
<td>0.005</td>
</tr>
<tr>
<td>Ferritin (ng/ml)</td>
<td>37.9±32.9</td>
<td>54.3±41.4</td>
<td>30-400</td>
<td>0.018</td>
</tr>
<tr>
<td>Folate (ng/ml)</td>
<td>6.5±2.7</td>
<td>9.7±12.1</td>
<td>4.5-32.2</td>
<td>0.012</td>
</tr>
<tr>
<td>Vitamin B12 (pg/ml)</td>
<td>275±135</td>
<td>382±295</td>
<td>191-663</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*NLR: neutrophil/lymphocyte ratio, *RLS: Restless Legs Syndrome

Figure 1: ROC Curve for NLR top redirect Restless Legs Syndrome. NLR was predictive at 1.58 with a 64% sensitivity and 50% specificity (CI: 95%, AUC: 0.648±0.05; 0.55-0.74).
Down syndrome (DS) is a chromosomal disorder resulted from trisomy human chromosome 21 (HSA21) and all DS patients exhibited cognitive impairment. Ts1Cje mouse model of DS has a triplicated region of mouse chromosome 16 (MMU16) which is homologous to HSA21. Three interferon receptor genes (Ifnar1, Ifnar2 and Ifngr2) are located at the triplicated region in MMU16 and also in HSA21. In this study, we aimed to determine the disrupted molecular networks and the role of the candidate gene in the neurogenic-to-gliogenic shift of Ts1Cje mouse brain. A functional transcriptome analysis was performed on the cerebral cortex, cerebellum and hippocampus of Ts1Cje mice at 4 time-points: postnatal day (P)1, P15, P30 and P84. Functional clustering analysis of the identified 317 differentially expressed genes reported interferon-related signaling networks as the most significantly dysregulated pathway in the Ts1Cje postnatal brain development. Both Ifnar1 and Stat1 were found over-expressed in P84 Ts1Cje cerebral cortex and cerebellum when compared to wild type littermates through qRT-PCR and western blotting analysis. Subsequently, the role of triplicated Ifnar1 was determined by treating Ifnar1 antagonist on differentiating neural stem cells derived from the SVZ of adult Ts1Cje. The assessment on the antagonistic effect of Ifnar1 antagonist reported successful attenuation on the aberrant Stat1, Sox1 and Tuj1 expression in the Ts1Cje group to an expression level which was similar to the wild type group. These findings, however, needs further validations to determine the relationship between overexpressed Ifnar1 and neurogenic-to-gliogenic shift mechanism in Ts1Cje mouse brain.
Aim: Chronic migraine causes a serious labor loss and disability in the society and increases the risk of depression and anxiety by negatively affecting the quality of life. The purpose of this study was to investigate the effects of OnabotulinumtoxinA (BoNT-A) treatment on efficacy before and after treatment in our cases with chronic migraine as well as depression, anxiety and disability caused by migraine.

Methods: According to the International Headache Classification (ICHD-III beta version), 60 adult patients who were diagnosed with chronic migraine were included in the study. A total of 155 IU BoNT-A treatment from 31 regions was administered in accordance with the protocol of PREEMPT study. Information about the characteristics of patients’ headaches, background and family history, drugs they used were recorded. Scores of Visual Analogue Scale, Migrain Disability Assessment Score (MIDAS), Beck Depression Inventory, and Anxiety Inventory scores were evaluated in the first month and in the third month before the procedure.

Results: BoNT-A injection provided a significant decrease in the number of days and severity of headaches, MIDAS disability scores and psychiatric complaints in cases with chronic migraine who did not respond to prophylactic treatments in the third month of the treatment.
Glioblastoma multiforme (GBM) is the most common and aggressive brain cancer with an extremely low 5-year survival rate. Stem cell related therapy has been attempted to attenuate tumorgenesis. However, the direct effects and the underlying mechanism are still undetermined. Here, C6 glioblastoma cells labeled with CM-Dil were co-cultured with rat embryonic neural stem cells (NSCs) in 2-D monolayer and 3-D spheres, then the proliferation, differentiation and invasion of C6 were detected to investigate the influence directly from NSCs. Results shown that the survival and proliferation of C6, which detected by cell counting and MTT assay respectively, were significantly decreased after 3 days co-culture with NSCs (P<0.05). The invasion ability of C6 was also significantly declined after 24 hours co-culture (P<0.05), as showed by the reduced number of viable cell underneath the membrane of transwell. However, no significant difference was observed between different groups in regarding to the total amount of GFAP+ cell, which indicating the status of C6 differentiation. Condition medium from NSCs was also applied and the similar results were obtained. Taken all these together, it suggested that NSCs could negatively regulate genesis and deterioration of GBM by directly inhibiting the survival, proliferation and invasion of tumor cell. Nevertheless, there is no significant change to the tumor maturation/differentiation. Detection of the effective signals from NSCs is currently ongoing. Our work based on NSCs could be a good approach for GBM treatment.
AOCN-0211
Session 02: Movement Disorder + Neurosciences (Current status in Stem Cell Therapy) + Headache and Pain

DOPAMINE AGONISTS VERSUS LEVODOPA AS INITIAL THERAPY IN PARKINSON’S DISEASE: DOSE COMPARISON AFTER LONG-TERM OF TREATMENT

W.T. Tang¹, C.P. Chong², G.B. Eow³
¹Universiti Sains Malaysia, School of Pharmaceutical Sciences, Kampar, Malaysia
²Universiti Sains Malaysia, School of Pharmaceutical Sciences, Penang, Malaysia
³Hospital Pulau Pinang, Department of Neurology, Penang, Malaysia

Objective: This study aimed to compare the mean levodopa equivalent dose (LED) requirement in both initial dopamine agonists and levodopa treated group after long term treatment.

Methods: This retrospective cohort study recruited patients with idiopathic Parkinson’s disease who were started with dopamine agonists or levodopa as initial therapy, and had more than 6 years of treatment. The highest tolerable drug dose was converted to LED using standardized conversion formulae and the mean LED in both treatment groups was compared at Year 6 to 10.

Results: A total of 126 patients were recruited, with 42 patients in initial dopamine agonist treated group and 84 patients in levodopa group. The difference of mean LED was not significant in Year 6 for both treatment groups, by using T-test analysis. However, the ANCOVA analysis showed that the initial dopamine agonists treated group had significantly higher mean LED (852.10 mg) than levodopa group (578.93 mg) in Year 7, with the adjustment of patients’ baseline characteristics (adjusted mean difference 95% CI 99.27-447.07 mg; \( p = 0.002 \)). The difference in mean LED was significantly sustained in Year 8, 9 and 10 (\( p < 0.05 \)).

Conclusions: As disease progresses over time, increment of antiparkinsonian medication dose is necessary to control the Parkinson symptoms. Higher LED requirement in dopamine agonist treated group may imply higher magnitude of disease progression, either in symptom severity or rate of progression. This may due to the different effects of levodopa and dopamine agonists on the compensatory mechanisms in early phase of Parkinson’s disease.
Session 03: Epilepsy
MICRORNAs AND EPILEPSY, A ROAD THAT IS STILL BEING PAVED: REVIEW

Ahmed Arafat¹, Fei Yin¹
¹Xiangya hospital - Central South University, Pediatrics neurology, Chang Sha, China

MicroRNAs and Epilepsy, A road that is still being paved: Review

Ahmed arafat¹, Fei Yin¹
¹Department of Pediatrics, Xiangya Hospital of Central South University, No. 87 Xiangya Road, Changsha, Hunan, 410008, China

dr.a.zaher@hotmail.com

corresponding author.

Yf2323@hotmail.com

Epilepsy is one of the most common neurological disorders, affecting approximately 65 million people worldwide. Over the past 6 years the association between Epilepsy and miRNAs has been a rich area of interest.

Objective: The object of this study was to evaluate the correlation between miRNA 301a-3p and miRNA-106b-5p and epilepsy.

Methods: In our paper, we report a systematic review of all published papers regarding the relation between miRNA 301a-3p and MiRNA-106b-5p and epilepsy.

Results: Six published reports of eligible studies meet the inclusion criteria, four studies involving 284 human participants and rats’ models have shown that miRNA 301a-3p was significantly dysregulated in Epilepsy with one study claiming that it had the best diagnostic value for Drug resistant epilepsy with 80.5% sensitivity and 81.2% specificity (Wang at el. 2015). Two studies involving 71 human participants have shown that miR-106b-5p was significantly dysregulated in Epilepsy with one study claiming that it had the best diagnostic value for epilepsy with 80.3 % sensitivity and 81.2 % specificity (Wang at el. 2015).

Conclusion: Although current evidences demonstrate that miRNA 301a-3p and MiRNA-106b-5p have a significant role in epilepsy, more evidence from advanced studies is needed, so we could save time and effort in our fight against Epilepsy.
EPINET - AN INTERNET-BASED PLATFORM TO FACILITATE CLINICAL RESEARCH IN EPILEPSY

J. Jayabal1, R. Frith1, E. Walker2, L. Sadleir2, W. D'Souza3, M. Tripathi4, P. Bergin1
1Auckland City Hospital, Neurology, Auckland, New Zealand
2Wellington Hospital, Paediatric Neurology, Wellington, New Zealand
3St. Vincent's Hospital, Neurology, Melbourne, Australia
4All India Institute of Medical Sciences, Neurology, New Delhi, India

Aim:

To establish a multi-centre, international database that will be used to obtain high quality evidence to guide the clinical management of epilepsy.

Method:

A secure international database has been constructed to systematically record information regarding patients with epilepsy, with the long term goals of:

1) conducting large, multi-centre, prospective, observational studies in people with a wide range of epilepsy syndromes and seizure types. Formal studies now underway include the first seizure, first AED and AED withdrawal registries;

2) conducting large, simple, pragmatic randomized controlled trials, such as the EpiNet-First trials, which are currently recruiting. Trials will be investigator-initiated and independent of pharmaceutical companies;

3) improving clinical care of patients. Although primarily for research purposes, the database is also designed to provide a useful clinical tool for clinicians, where information entered can be communicated effectively to patients and their primary physicians.

Results:

As of Jan 2016, there are more than 8700 patients in the EpiNet database from more than 20 countries. The top three participating cities in Asia-Oceania have been Auckland (2562 patients), Melbourne (2492) and New Delhi (534).

Conclusion:

The EpiNet database has been developed with the assistance of neurologists and epileptologists from many countries, including those from the Asia-Oceania region. We would encourage more clinicians from Asia-Oceania to participate in this project. The database can be used for local or regional studies, as well as major international studies. We are confident that EpiNet can provide us all with groundbreaking information into the optimal management of patients with epilepsy.
EFFICACY AND SAFETY OF ADJUNCTIVE EVEROLIMUS THERAPY IN ASIAN PATIENTS WITH REFRACTORY PARTIAL-ONSET SEIZURES ASSOCIATED WITH TSC IN EXIST-3

J. Lawson¹, Z. Yapıcı², H. Ikeda³, T. Polster⁴, P.C. Fan⁵, R. Nabbout⁶, P. Curatolo⁷, P.J. de Vries⁸, N. Berkowitz⁹, M. Voï¹⁰, S. Peyrard¹⁰, A. Vaury¹⁰, D.N. Franz¹¹
¹Sydney Children’s Hospital, Neurology, Randwick, Australia
²Istanbul University, Department of Neurology, Istanbul, Turkey
³Shizuoka Institute of Epilepsy and Neurological Disorders, National Epilepsy Center, Shizuoka, Japan
⁴Mara Hospital- Bethel Epilepsy Center, Paediatric Epileptology, Bielefeld, Germany
⁵National Taiwan University Hospital, Department of Pediatrics, Taipei, Taiwan
⁶Hospital Necker Enfants Malades, Department of Pediatric Neurology, Paris, France
⁷Tor Vergata University Hospital, Child Neurology and Psychiatry Unit, Rome, Italy
⁸University of Cape Town, Division of Child and Adolescent Psychiatry, Cape Town, South Africa
⁹Novartis Pharmaceuticals Corporation, Oncology, New Jersey, USA
¹⁰Novartis Pharmaceuticals S.A.S, Statistics, Rueil-Malmaison, France
¹¹Cincinnati Children’s Hospital Medical Center, Department of Neurology, Ohio, USA

Background

EXIST-3 evaluated the efficacy and safety of everolimus 3-7 (low trough [LT]) and 9-15 ng/mL (high trough [HT]) concentrations (C_min) against placebo in a global study of 366 patients with refractory partial-onset seizures (POS) associated with tuberous sclerosis complex. In a post-hoc analysis, patients of Asian race/ethnicity were evaluated, given potential varied responses to antiepileptic drugs attributed to pharmacogenetic variations.

Method

Patients aged 2-65 years were randomized to everolimus LT/HT C_min or placebo. The primary endpoint, which was met and previously reported, was change in average weekly frequency of POS from baseline, expressed as percentage reduction and response rate (RR; ≥50% reduction); denoted as percentage; 95% confidence interval (CI).

Results

Among 366 patients, 87 were Asians (9 countries) — 29 were randomized to LT, 31 to HT, and 27 to placebo. Median percentage reduction in seizure frequency was greater with LT (40.5%; 13.0-48.1), HT (34.9%; 13.3-63.6) vs placebo (6.0%; -14.0 to 30.0%). RR with LT was (31%; 15.3-50.8), HT (35.5%; 19.2-54.6) vs placebo (18.5%; 6.3-38.1%). Most common (≥20%) all-grade adverse events (AEs) reported with LT/HT vs placebo included stomatitis (55.2%/41.9% vs 7.4%), mouth ulceration (37.9%/35.5% vs 7.4%), vomiting (20.7%/3.2% vs 0), nasopharyngitis (24.1%/29% vs 11.1%), and upper respiratory tract infection (24.1%/29% vs 22.2%). Grade 3 or 4 AEs were reported in 17.2%/9.7% vs 7.4%. Despite the limitations of smaller sample size, the clinical and adverse effects of everolimus in Asians resemble that reported for the overall population.
Conclusion

Adjunctive everolimus therapy displayed similar efficacy in improving POS in an Asian subgroup, with no new safety concerns.
GENDER ASPECTS OF RESISTANT EPILEPSY IN WOMEN
G. Odintsova¹, A. Figol¹, K. Abramov¹, A. Chugunova²
¹Federal Almazov North-West Medical Research Centre, neurosurgery, St. Petersburg, Russia
²Federal Almazov North-West Medical Research Centre, reproductive technology, St. Petersburg, Russia

Purpose: To study gender aspects of resistance in women with epilepsy

Method: The work was part of prospective observation uncontrollable research of antiepileptic drugs (AEDs) side effects on reproductive health (RH) in 155 women into 3 groups: 1gr. - AEDs monotherapy, 2 gr. - polytherapy, 3 gr. - without AEDs. Epilepsy onset, catamenial epilepsy, reproductive complications were investigated

Results: Average age made 25 years. 1gr. included 68 patients (44%), 2gr. - 67 (43%), 3gr. - 20 women (13%). Epilepsy onset before puberty- 1-9y.o. were in 15%, in puberty- 10-18y.o. 59%, after puberty- older 18-26%. Differences were statistically significant above in puberty (p <0,001). Prevalence of epilepsy onset in the integrated age range of 12-16 years was statistically reliable (p<0,001). The general indicator of a catamenialnost in cohort made 32%. Dominance of the catamenial epilepsy was noted into 2 group (43%) in comparison with 1(24%) and 2 (25%) groups. Differences were statistically significant above at polytherapy group (p <0,001). The frequency of reproductive endocrine complications made 53%. Reproductive disturbances due to AEDs made 40%. AEDs polytherapy enlarged the frequency of reproductive disturbances in comparison with other groups and made 60% (p <0,001)

Conclusion: Gender aspects of resistant epilepsy were caused by sexual hormones influence on epileptogenesis. The epilepsy onset occurred more often during the periods of the beginning oesstradiolum production and its ovulatory peaks. It confirms proconvulsive effect by estrogens. catamenial epilepsy was a predictor of resistance. Reproductive complications were frequent side effect of antiepileptic therapy and took part in disease resistant
NLRP1 inflammasome is activated in patients with temporal lobe epilepsy and contributes to neuronal pyroptosis in amygdala kindling-induced rat model

C.C. Tan, J.T. Yu, L. Tan

1Qingdao Municipal Hospital East, Neurology, Qingdao, China

Temporal lobe epilepsy (TLE) is often characterized pathologically by severe neuronal loss in the hippocampus. Understanding the mechanisms of neuron death is a key for preventing the neurodegeneration associated with TLE. However, the involvement of neuronal loss to the epileptogenic process has yet to be fully determined. Recent studies shown that the activation of NLRP1 can generate a functional caspase-1-containing inflammasome in vivo to drive the proinflammatory programmed cell death termed “pyroptosis”, which have key roles in the pathogenesis of neurological disorders. To the best of our knowledge, there are no reported studies that performed a detailed identification and validation of NLRP1 inflammasome during the epileptogenic process. Here, we compared expression of NLRP1 and caspase-1 in resected hippocampus from patients with intractable TLE to matched control samples. Western blotting detected up-regulated NLRP1 levels and active caspase-1 within TLE patients than controls, suggesting a role for this inflammasome in TLE. Moreover, we employed direct in-vivo infusion of nonviral small interfering RNA to knockdown NLRP1 or caspase-1 in amygdala kindling-induced rat model, and discovered that these NLRP1 or caspase-1 silencing rats resulted in significantly reduced neuronal pyroptosis and seizure frequency and severity. Our data suggest that NLRP1/caspase-1 signaling participates in the seizure-induced degenerative process in human and animal model of TLE, and point to the silencing of NLRP1 inflammasome as a promising strategy for TLE therapy.
PREOPERATIVE MRI CAN PREDICT STEREOTACTIC RADIOFREQUENCY THERMOCOAGULATION OF THE AMYGDALOHIPPOCAMPAL COMPLEX OUTCOMES IN THE TREATMENT OF MEDIAL TEMPORAL LOBE EPILEPSY
Q. Zhao
1306 Hospital of PLA, Neurosurgery, Beijing, China

Purpose To explore the therapeutic efficacy of depth-electrode-guided stereotactic radiofrequency thermocoagulation (RFTC) of the amygdalohippocampal complex for the treatment of intractable medial temporal lobe epilepsy (MTLE) between MRI negative and positive patients.

Methods A total of 127 cases of MTLE were retrospectively studied after depth-electrode-guided RFTC of the amygdalohippocampal complex. A preoperative MRI scan (T1, T2, Flair sequence) was performed in all patients, in which 67 cases were positive for brain lesions and 60 cases were negative.

Results After 24–83 months follow-up, 54.69% (70/127) of patients were in Engel class I–III, with 32.28% (41/127) of patients in Engel class I. A total of 50.00% (30/60) of patients in the MRI-negative group became seizure-free after treatment, but only 16.42% (11/67) of cases in the MRI-positive group were seizure-free at the time of follow-up. A significant difference in seizure-free outcome (P < 0.001) was obtained between the MRI-positive and MRI-negative groups.

Conclusion MTLE patients with a preoperative MRI scan negative for lesions show better seizure control after RFTC of the amygdalohippocampal complex than MRI-positive patients. RFTC of the amygdalohippocampal complex significantly reduces epileptic discharges, but does not thoroughly deal with structural lesions observed by MRI. MRI-positive MTLE patients show better results with surgical resection, and therefore, must be carefully selected for RFTC of the amygdalohippocampal complex.
THE PRIMARY STUDY OF HIPPOCAMPAL TRANSACTION FOR THE TREATMENT OF MEDIAL TEMPORAL LOBE EPILEPSY

Q. Zhao

1306 Hospital of PLA, Neurosurgery, Beijing, China

Objective To evaluate the effect of seizure control and memory protection of hippocampal transaction for the treatment of medial temporal lobe epilepsy.

Methods Five patients with medial temporal lobe independent ictal discharges were treated with hippocampal transection, in which 2 were in left side, 2 were in right side and the rest 1 was transected in both side by stages. The neuropsychological studies were performed for these patients before and after operation to evaluate the affect of IQ and memory function. The outcomes of seizure control were obtained by telephone calls.

Results The follow up time was 9 to 16 months. Seizure free (Engel I) was obtained in 3 cases (in which 1 case was reduced seizure frequency in 50% after one side transection but seizure free after the transection of another side by stages). One case was reduced seizure frequency more than 50% (Engel III) and the rest 1 was no change (Engel IV). Four cases were undergone entire pre and postoperative examinations of neuropsychology and no deficits were found in IQ and memory.

Discussion Hippocampal transection can either spare the memory function of hippocampus or control seizures. Especially in bilateral temporal lobe epilepsy, if the other side would still be the epileptogenic focus after one side transection, the transection of other side could be performed by stages. However, because of the less of cases, the further observation should be performed by the accumulation of cases.
Session 04: Neuropaediatrics/tumor
RISK FACTORS FOR DYSKINETIC FORM OF CEREBRAL PALSY
G. Mukhambetova¹, A. Karimova¹, K. Chepaikina², G. Akhanova², T. Varzina²
¹Kazakh National Medical University, Neurology Department, Almaty, Kazakhstan
²Kazakh National Medical University, Internship Department, Almaty, Kazakhstan

Objective: To determine the effects of prolonged conjugational icterus on the development of dyskinetic form of cerebral palsy.

Material and Methods: We studied 35 children with dyskinetic form of cerebral palsy at the age from 1 year to 7 years, who received rehabilitation program in Republican Child Rehabilitation Center "Balbulak". By gender boys were 54.29% (19 cases), girls 45.71% (16 cases). We reviewed the anamnesis with the definition of risk factors for cerebral palsy: hypoxia, intrauterine infection, prolonged conjugational hyperbilirubinemia; progress of pregnancy and childbirth; duration of icterus and the level of indirect bilirubin. Patients with prolonged icterus were examined by enzyme immunoassay blood test for fetal infections - herpes simplex virus type 1, type 2, cytomegalovirus, toxoplasmosis.

Results: Analysis of anamnestic pre and perinatal data showed a combination of several risk factors: acute and chronic hypoxia (62.86%), premature birth (51.43%), perinatal hemorrhagic stroke (5.71%). In the postnatal period, prolonged icterus was diagnosed in 60% of patients. It manifested itself since 3 days of life and held for an average up to 2.24 ± 0.43 months. Level of indirect bilirubin increased in the range from 190 to 400 mmol/l. Enzyme immunoassay blood test revealed the activity of infection with increased Ig A for cytomegalovirus in 11.43% of patients, IgG for cytomegalovirus and herpes simplex viruses (14.29%).

Conclusion: The impact of hyperbilirubinemia on the development of dyskinetic form of cerebral palsy in children is possible with a combination of several factors.
THE USE OF TARGETED CAPTURE AND MASSIVELY PARALLEL SEQUENCING IN ATYPICAL LEUKOENCEPHALOPATHY

J. PENG

xiangya hospital, The department of child neurology, chang sha, China

Objective: To assess the utility and effectiveness of targeted capture and sequencing in atypical leukoencephalopathy patients.

Methods: A multicenter retrospective study of 48 patients with atypical leukoencephalopathy was performed. These patients were recruited into our cohort according to the strict inclusion and exclusion criteria, then we screened for them using the personalized chip containing 118 genes reported to be associated with leukoencephalopathy and made the validation among their parents using Sanger sequencing.

Results: A total of 39.6% (19/48) of the patients exhibited pathogenic mutations. Including four associated with metachromatic leukodystrophy, three associated with vanishing white matter leukoencephalopathy, three associated with mitochondrial complex I deficiency, one associated with globoid cell leukodystrophy, two associated with megalencephalic leukoencephalopathy with subcortical cysts, two associated with Pelizaeus-Merzbacher disease, one associated with X-linked adrenoleukodystrophy, one associated with Zellweger syndrome, one associated with amyotrophic lateral sclerosis and one associated with Alexander disease. In this study, fourteen pathogenic mutation sites were identified for the first time.

Conclusion: Our data supported the combination of targeted capture and massively parallel sequencing technology with clinical and genetic diagnosis, allowing the identification of atypical leukoencephalopathy, highlighting its usefulness for rapid and comprehensive genetic testing in the clinical. These results expand our knowledge of the genetic and clinical spectra of leukoencephalopathy.

Classification of evidence: This study provides Class IV evidence that targeted capture and massively parallel sequencing enables the identification of pathogenic mutations in atypical leukoencephalopathy.
Intellectual developmental disorder (IDD) is at present the primary disabling cause in Chinese children, which seriously affects the quality of the patients’ life. However, because of different social and economic environments from western countries, the data of high risk factors and etiological characteristics are lacking in Chinese populations. In this study, we conducted a prospective study in 103 Chinese children with different severity of IDD through medical history collection, metabolic screening, karyotype analysis, and relevant molecular tests. Patients were divided into two groups according to Development Quotient (DQ) or Intelligence Quotient (IQ): mild (51-69) and severe (≤50). Results showed that the group of children with mild IDD accounted for 71.8% (74/103). About 16.5% (17/103) of the IDD children were affected by perinatal factors. Maternal history of abnormal pregnancy and adverse family history were two of the highest risk factors in IDD children, especially severe IDD children. Children were more prone to develop severe mental retardation if there was consanguineous marriage or unexplained death or mental disorder or epilepsy within three generations (p < 0.05). The etiological diagnosis rate of patients with severe IDD was 96.6%. Chromosomal abnormalities are the most common genetic risk factors of IDD, accounting for 28.2% (29/103). This study addressed the importance of high risk factors and etiological characteristics of IDD with different severity, which is critical to take corresponding steps including strengthening pregnancy care and high-risk maternal labor monitoring to improve early intervention of IDD patients in Chinese population.
Session 05:

CNS infection
AOCN-0034
Session 05: CNS infection

THE ROLE OF MRI PARAMETERS AS PROGNOSTIC MARKERS IN THE OUTCOME OF SOLITARY CYSTICERCUS GRANULOMA
L. Aggarwal¹, G. Singh¹, K. Saggar², G.S. Dhuria³
¹Dayanand Medical College and Hospital, Neurology, Ludhiana, India
²Dayanand Medical College and Hospital, Radiology, Ludhiana, India
³Dayanand Medical College and Hospital, Paedetrics, Ludhiana, India

Background: Solitary cysticercus granuloma (SCG) represents a degenerating single cerebral cysticercus cyst; is a common presenting form of Neurocysticercosis, particularly in India and United States; and may cause refractory seizures. Because of the epidemiologic importance of SCG, an optimal magnetic resonance imaging (MRI) prognostic protocol is vital, and advanced MRI techniques have recently been used in this context. Objective: To study selected MRI parameters as prognostic markers in the outcome of resolution of SCG.

Material and Methods: Patients with seizures and demonstrating intracranial SCG, diagnosed as per the revised clinical and radiological (MRI) diagnostic criteria for SCG, over a period of one year were subjected to non-conventional MRI evaluation including diffusion weighted imaging (DWI) with apparent diffusion coefficient (ADC) calculation; proton magnetic resonance spectroscopy (MRS) and magnetization transfer imaging (MTI). Six months follow up MRI scan was done. The association of various advanced MRI techniques in predicting the resolution of the SCG was analyzed. Results: MRI features which favoured the trend towards resolution of the SCG lesion were a lower N-Acetylaspartate/Choline (NAA/Cho) ratio and higher Choline/Creatine (Cho/Cr) as well as N-Acetylaspartate/Creatine (NAA/Cr) ratios on MRS, absence of perilesional gliosis and absence of seizure recurrence; with higher Cho/Cr and NAA/Cr ratios on MRS reaching a statistical significance. Conclusion: MRI is the investigation of choice for determining the prognostication of SCG. Advanced MRI techniques are complementary to conventional MRI for this purpose. However larger prospective studies with a longer duration of follow-up are needed to statistically establish the above observations.

Table 1

<table>
<thead>
<tr>
<th>Role of MR Spectroscopy in predicting the resolution of SCG*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameters</td>
</tr>
<tr>
<td>------------</td>
</tr>
<tr>
<td>MR Spectroscopy (lesional median values)</td>
</tr>
<tr>
<td>No. of Pat.</td>
</tr>
<tr>
<td>NAA §</td>
</tr>
<tr>
<td>Cr§</td>
</tr>
<tr>
<td>NAA/Cho</td>
</tr>
<tr>
<td>NAA/Cr</td>
</tr>
<tr>
<td>Cho/Cr</td>
</tr>
</tbody>
</table>

*excluding 3 patients lost to follow up; CR stands for complete resolution; PR for partial resolution; NR for no resolution; Pat. stands for patients; §NAA stands for N-acetyl aspartate; Cho for Choline; Cr for Creatine; ANOVA method.
Table 2

Percentage of seizure recurrence in SCG according to resolution of lesions

<table>
<thead>
<tr>
<th>Seizure recurrence</th>
<th>CR†</th>
<th>SCG</th>
<th>PR†</th>
<th>NR†</th>
<th>Total no. (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>8 (100)</td>
<td>17 (70.83)</td>
<td>3 (60)</td>
<td>28 (75.68)</td>
<td>0.170</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
<td>7 (29.17)</td>
<td>2 (40)</td>
<td>9 (24.32)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* excluding 3 patients lost to follow up; †CR stands for complete resolution; PR for partial resolution; NR for no resolution.

Table 3

Seizure recurrence in SCG according to perilesional gliosis

<table>
<thead>
<tr>
<th>Total no. of cases (N=9*)</th>
<th>Persistent seizures</th>
<th>No seizures</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gliosis (n=2)</td>
<td>1 (50%)</td>
<td>1 (50%)</td>
<td>0.284</td>
</tr>
<tr>
<td>No gliosis (n=7)</td>
<td>1 (14.3%)</td>
<td>6 (85.7%)</td>
<td></td>
</tr>
</tbody>
</table>

*excluding two cases lost to follow up

Figure 2. Left Temporal SCG with no resolution

A. T2W image shows a small hypointense area and minimal perilesional edema.

B. The perilesional hypointensity better demonstrated (yellow arrow) on T1-MT images is seen to extend beyond the abnormality (red arrow) seen on T2-W images and is suggestive of perilesional gliosis.

Patient had no resolution of the lesion on follow up imaging.
Background: Tuberculous meningitis (TBM) is a growing problem in developing countries, where data is scarce in our local setting. Our objectives were to analyze the incidence, clinical features, prognostic factors and outcomes of patients with TBM.

Methods: All patients with TBM who were admitted to UKMMC from 2003 to 2015 were analyzed. Demographic data, clinical data and laboratory features were obtained. Univariable cox regression analysis were used to identify the variables associated with survival. Survival analysis was estimated using the Kaplan–Meier method.

Results: We included 61 cases (mean age 47.4 years, 60.7% male). More than 70% of our patients presented with headache, altered conscious level, neck stiffness and focal neurological signs. Majority of the cerebrospinal fluid (CSF) analysis showed low lymphocyte predominant cells, high protein concentration and low CSF to serum glucose ratio. Only 9.8% had a positive CSF Polymerase Chain Reaction. Leptomeningeal enhancement, cerebral infarctions and hydrocephalus were features found on cranial imaging. The good prognostic factors in this study were photophobia, better Glasgow Coma Score and lower Modified Rankin Scale. Poor prognostic factors were intubation, surgical procedures, high CSF protein concentration and tuberculoma. The overall survival during hospitalisation was 86.9% and at 6 months was 70.5%; the survival rate for HIV patients were 87% and 68.5% during hospitalisation and at 6 months respectively.

Conclusions: The clinical presentations of TBM were usually non-specific especially in the presence of other co-infection. Hence, a strong clinical suspicion should be maintained, coupled with adequate CSF analysis and radiological imaging.
Object: Hydrocephalus induced by acute bacterial meningitis (BMH) remains a relatively common and potentially fatal condition in childhood. Studies about ventriculoperitoneal shunt (VPS) surgery treatment are few. The aim of this study is to evaluate the clinical role of VPS surgery for BMH patients.

Methods: Cases of BMH were collected over five years (2010-2015) from patients of Xiangya 1st hospital (a large teaching medical center in China). The data included clinical features at admission, treatment, post-surgery statement and neuropsychological sequelae during the follow-up period.

Results: 15 BMH infants (including 7 preterm babies) were included. All were classified as obstructive hydrocephalus except for 4 patients were communicating hydrocephalus. The interval (time elapsed) from the initial symptoms to VPS surgery was 4.2 months. Those cases who have had their CSF features adjusted have suffered less surgery complications (only 1 patient) while for those whom their CSF features were failed to be adjusted have shown 5 patients with post-surgery complications. At the end of our extensive follow-up, 13 patients have survived with morbidity rate of 13.3%. 6 patients have had a fair outcome and 7 have shown complete recovery.

Conclusion: VPS surgery is an effective method to relieve the pressure caused by hydrocephalus among neonates and infants. The control of intracranial infection prior to surgery is the key to reduce postoperative complications. Long-term post-operative management will be only accomplished with parents and patients comprehensive cooperation.
Introduction: Symptomatic neurosyphilis (NS) can have varied presentation with syndromes suggestive of meningitis, meningo-vascular and parenchymatous involvement. It rarely presents in its classical form of tabes dorsalis or general paresis, but present with atypical forms. Aims: To evaluate different types of clinical presentations of NS. Results: Clinical profile of 38 cases of NS diagnosed in the Department of Neurology, Gauhati Medical College between August 2008 to January 2016. There were 33 male and 5 female with age of 17 to 63 years. 17 cases presented with Neuropsychiatric symptoms in the form of dementia, behavioral abnormalities and chronic psychosis; Extra pyramidal features in 1; Encephalitis like symptoms 6; stroke 3; optic neuritis 2; 9 myelopathy in the form of transverse myelitis and motor neuron disease like presentation. 29 cases had reactive VDRL in blood and 9 having nonreactive VDRL but reactive TPHA in serum. CSF VDRL was positive in 30 cases, raised protein in 29 and lymphocytic pleocytosis found in 17 patients. ELISA for HIV was negative in all cases. 31 cases fulfilled the criteria of definitive NS and 7 of presumptive NS. All except 2 received injection procaine penicillin for 14 days. Two patients were on antipsychotic drugs developed NMS (Neuroleptic Malignant Syndrome) during treatment. Patient with myelitis received a course of steroid. Conclusion: Syphilis can have neurological involvement at different sites of neuraxis. High index of clinical suspicion is required to diagnose NS in patients with history of promiscuous behaviour.

Keywords: neurosyphilis, neuropsychiatric features, VDRL, TPHA
INTRODUCTION

Tuberculous meningitis (TBM) is associated with high morbidity and mortality and is a common infectious disease entity encountered in developing countries such as Sri Lanka.

OBJECTIVES

To analyze the demographic pattern, investigation findings, and complications of the patients diagnosed to have TBM in a tertiary care hospital in Sri Lanka.

METHODS

A retrospective cross-sectional study design was utilized among patients fulfilling the standard consensus case definition of TBM over a period of three years from 2012-2015. The demographical pattern, clinical features, CSF findings imaging results were analyzed.

RESULTS

A total of 72 patients were included. Mean age at diagnosis was 40.25 +/- 16.4 years. A male preponderance was noted (58.3%). Twenty patients (27.8%) had systemic symptoms. Focal neurological signs and cranial nerve palsies were present in 33 (45.8%) and 31 (43.1%) respectively.

An elevated CSF cell count with lymphocytic predominance was noted in 39 patients (54.2%). Elevated protein and decreased sugar were found in 38.9% (28) and 40.4% (32) respectively, and TB PCR was positive in three patients. None of the patients had a microscopic confirmation of TB from CSF or extraneural tissue.

Basal meningeal enhancement, hydrocephalus, and infarction were found in 5 patients each (6.9%) and tuberculoma was seen in 8 patients (11.1%) in MRI brain.

CONCLUSIONS

A low microbiological yield is noted in patients with TBM in this study population with few patients demonstrating radiological evidence of the disease. Clinical and CSF criteria were utilized in most patients for the diagnosis, following exclusion of alternative diagnoses. This highlights the diagnostic restrictions of TBM in resource-limited settings.
Session 6: Neuromuscular/Neurophysiology
A STUDY ON OPTIMAL CONCENTRATIONS OF ISODIOSPYRIN PUTATIVE INHIBITORY ACTIONS AGAINST EXONIC SPlicing ENHANCERS OF DYSTROPHIN GENE EXON 53 SKIPPING IN DUCHENNE MUSCULAR DYSTROPHY

H. Alzahrani¹, D.M. Mustapha², D.T. Sasongko³
¹, Riyadh, Kingdom of Saudi Arabia
²Universiti Sains Malaysia, Neuroscience, Kota Bharu, Malaysia
³Universiti Sains Malaysia, Genetics, Kota Bharu, Malaysia

Introduction: Duchene muscular dystrophy (DMD) is an X-linked recessive disorder. It is characterized by rapid loss of muscular tissues due lacking gene of muscle replacement. The DMD gene is responsible for Dystrophin protein expression, which exists within a complex called Dystrophin glycol-protein complex (DGC). Exon mutations within DMD gene cause defective expression of Dystrophin. This study aimed to determine the inhibitory actions of Isodiospyrin targeting splicing factors and SR protein (Serine-arginine rich amino acids) a known topoisomerase inhibitor, which plays a critical role in splice site selection. Previous studies demonstrated that Isodiospyrin has antitumor activity and inhibited topoisomerase enzyme from phosphorylating SF2/ASF splicing factor. In the current study we used plasmid of non-mutated exon 53 minigenes, transfected into non-mutated HEK-293 cell lines. Then, observe its actions on cells viability and exon splicing modification. This was tested using RT-PCR, followed by exon 53 sequence confirmation analysis software.

Results: In consistence with previous studies, concentration of half maximal inhibitory effect (IC50) was 3.58μM, and the optimal inhibitory concentrations were: 1.79, 0.90, and 0.60μM. However, there was no detection of exon 53 skipping when exposing non-mutated HEK-293 cells to the optimal concentrations of Isodiospyrin compound.

Conclusion: The results suggest that exon 53 splicing may occur without phosphorylation of SR proteins targeted by Isodiospyrin, which indicated that the splicing of exon 53 is ESE-independent in non-mutated HEK-293 cells.
Objective: Motor nerve conduction studies have low sensitivity in the electrodiagnosis of CTS. MUNE is a new electrodiagnostic technique. This study aims at finding the utility of MUNE in the electrodiagnosis of CTS.

Background: In CTS diagnostic confirmation is often based on the electrodiagnostic data. The sensitivity and specificity of conventional electrodiagnostic studies is 80.2 (71.389.0) and 78.7 (66.491.1) respectively. The role of MUNE in CTS is not well studied.

Methods: Study subjects included 37 patients with 68 symptomatic hands who met the clinical diagnostic criteria of American Academy of Neurology (AAN) and 32 healthy controls. In addition to conventional electrodiagnostic (AAN criteria) tests, MUNE was studied in abductor pollicis brevis (APB).

Statistical analysis included conventional tests, ANOVA, post hoc correlation coefficient and area under ROC curves.

Results: Of 68 symptomatic hands, 64 (94%) hands met the AAN electrodiagnostic criteria of CTS. Whereas decrease in number of motor units (MUs) on MUNE in APB observed was observed in 66 (96%) hands as compared to controls. Of the 46 (71%) hands with normal CMAP, 20 (43%) had decreased number of MUs on MUNE in APB. There was linear relation between motor latency and MUNE abnormalities. The sensitivity and specificity for various parameters were: 114.5 for MUNE (sensitivity 98.5%, specificity 96.7%); 10.95 mV for CMAP amplitude (sensitivity 73.1%, specificity 65.6%); for difference in palmar median and ulnar sensory latency (sensitivity 90%, specificity 88%).

Conclusion: Our study suggests MUNE adds to the electrodiagnostic evaluation of early CTS with a high diagnostic sensitivity and specificity.
Background: Myasthenia Gravis is an autoimmune neuromuscular disorder characterized by the production of abnormal autoantibodies against receptors in the neuromuscular junction. It has been the practice to offer thymectomy in all generalized Myasthenia gravis patients despite the lack of robust evidence.

Objectives: The objectives of this study are to describe the clinical profile and differentiate the clinical outcomes of thymectomy versus non-thymectomy, and thymomatous versus non-thymomatous Myasthenia Gravis patients in the Philippine General Hospital.

Methodology: A total of 69 post-thymectomy and 16 non-thymectomy patient records were successfully retrieved. The demographic characteristics, surgical approach and histopathologic results were obtained. The clinical outcome after follow-up was also determined and grouped according to the following: 1) complete remission, 2) pharmacological remission, 3) no clinical change 4) worsening symptoms and 5) mortality.

Results: Majority of patients were females (68.0%) with a mean age of 39.8 years and a mean duration of myasthenic symptoms of 21 months. Using the MGFA classification, 54.1% of patients fell under Class II and 48.2% of them presented with generalized weakness. In this study, 60.8% of post-thymectomy Myasthenia gravis patients had either complete remission or pharmacologic remission compared to 12.5% among non-thymectomy patients (p-value <0.001). No significant difference in the clinical outcome was found between thymomatous and non-thymomatous Myasthenia gravis after thymectomy (p-value 0.29).

Conclusion: This study showed that both thymomatous and non-thymomatous Myasthenia gravis patients who underwent thymectomy had a higher incidence of complete stable remission and pharmacologic remission as compared to Myasthenia gravis patients who did not undergo thymectomy.
Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder characterized by a selective loss of motor neurons in the brain and spinal cord. Multiple toxicity pathways, such as oxidative stress, misfolded protein accumulation, and dysfunctional autophagy, are implicated in the pathogenesis of ALS. However, molecular basis of the interplay between such multiple factors in vivo remains unclear. Here, we report that two independent ALS-linked autophagy-associated gene products; SQSTM1/p62 and ALS2, but not antioxidant-related factor; NFE2L2/Nrf2, are implicated in the pathogenesis in mutant SOD1 transgenic mouse ALS models. We generated SOD1H46R transgenic mice either on a Nfe2l2-null, Sqstm1-null, or Sqstm1/Als2-double null background. Loss of SQSTM1 but not NFE2L2 exacerbated disease symptoms. A simultaneous inactivation of SQSTM1 and ALS2 further accelerated the onset of disease. Biochemical analysis revealed that loss of either SQSTM1 or ALS2, or both of them, increased the level of insoluble SOD1 in the spinal cord. Remarkably, histopathological examinations revealed that loss of SQSTM1 resulted in accelerated motor neuron degeneration with accompanying the preferential accumulation of ubiquitin-positive aggregates in spinal neurons. Thus, SQSTM1 and ALS2 can additively modulate the disease phenotypes, whereas the NFE2L2-mediated antioxidant pathway plays a minor role in the pathogenesis. We here propose that two ALS-linked factors, SQSTM1 and ALS2, have cumulative protective roles against mutant SOD1-mediated toxic insults possibly via modulating the autophagy-endolysosomal system.
VITAMINS DEFICIENCIES AND NEUROPATHY AMONG MYANMARESE REFUGEES IN TWO MALAYSIAN TERTIARY CENTRES

F.L. Hiew¹, I. Looi², S. Viswanathan¹, S. Datuk Puvanarajah¹, M.H. Rafia¹
¹Kuala Lumpur Hospital, Neurology, Kuala Lumpur, Malaysia
²Hospital Seberang Jaya, Neurology, Seberang Jaya, Malaysia

Background: Vitamins deficiency is prevalent among displaced refugees, leading to various health problems including subacute-onset peripheral neuropathy. Since 2008, Malaysia as a country receiving refugees under the resettlement programme has documented newly-arrived Myanmarese refugees admitted for subacute-onset peripheral neuropathy. This neuropathy phenotype is less well described.

Objective: This study aimed to present the neuropathy findings from a cohort of Myanmarese refugees with prior history of starvation at 2 neurology centres in Malaysia (Kuala Lumpur and Seberang Jaya Hospital) between 2008-2014.

Methods: Detailed clinical neurological and electrophysiological data were collected alongside correlating biochemical evidence of various nutritional deficiencies.

Results: Thirty-nine patients with clinically confirmed subacute-onset peripheral neuropathy were assessed; mean duration of starvation before symptoms onset, corresponded to travelling period was 57.9 days; mean age 23.2 years; 97% male. Mean length of stay 13.5 days. All had axonal polyneuropathy, majority of mixed sensori-motor (30/39), confirmed by electrophysiology study. A severe, distal motor neuropathy was the predominant phenotype, manifested clinically as foot (56%) and wrist drop (18%). A subset of patients had associated central nervous system involvement (10/39). A significant proportion demonstrated measurable vitamins deficiencies; folate (20/27), vitamin B12 (17/32) and thiamine (1/2). Mean MRC sum score improvement of 3.8 was observed over a relatively short in-patient stay in 18/29 following vitamins supplementation and supportive therapy.

Conclusion: Vitamins deficiency is an important health issue among refugees. The description of subacute-onset axonal polyneuropathy following period of starvation should aid early screening and diagnosis as well as contributing to the understanding of its treatment.
<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Rohingya</th>
<th>20 (51%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chin</td>
<td>17 (44%)</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>2 (5%)</td>
</tr>
<tr>
<td><strong>Neuropathy subtype</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed sensori-motor axonal neuropathy</td>
<td>30 (75.7%)</td>
<td></td>
</tr>
<tr>
<td>Pure motor axonal neuropathy</td>
<td>8 (20.5%)</td>
<td></td>
</tr>
<tr>
<td>Pure sensory axonal neuropathy</td>
<td>1 (2.8%)</td>
<td></td>
</tr>
<tr>
<td><strong>Associated nutritional deficiency</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microcytic anaemia</td>
<td>18 (46%)</td>
<td></td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>11 (28%)</td>
<td></td>
</tr>
<tr>
<td><strong>CSF study</strong></td>
<td>Normal result</td>
<td>26/27 (96%)</td>
</tr>
<tr>
<td><strong>Mean MRC sum score (/60) (SD)</strong></td>
<td>Admission: 18.7 (6.5)</td>
<td>Discharge: 22.5 (5.7)</td>
</tr>
</tbody>
</table>
Charcot-Marie-Tooth disease (CMT) is the most common inherited peripheral neuropathy. It has been associated with mutations in more than 80 genes and loci but almost half of CMT patients are still waiting to uncover their genetic causes. In the present study, we analyzed the prevalence of causative mutations identified by traditional methods and Whole-exome sequencing (WES) in 1,291 Korean patients. Genomic DNA from 805 unrelated Korean CMT families was screened for mutations in the coding regions of the PMP22, MFN2, Cx32, and MPZ gene. WES was applied to identify causative mutations using the Human SeqCap EZ Human exome library, v2.0 and the Solexa GAIIx Genome Analyzer. Through whole exome sequencing, we identified 136 causative mutations from 46 genes including 69 novel mutations and rate of mutation identification was higher than previous (45.1 %). In the whole cohort, the PMP22 gene duplication accounts for the majority of molecularly diagnosed families (34.8 %). Mutations of GJB1, MFN2, and MPZ accounted respectively for 10.9, 6.4, and 4.1 % of families with an inherited peripheral neuropathy. Causative mutations of 356 patients from 330 families (41.0 %) were not identified and the rate of de novo mutations was 12.6 %. In addition, clinical heterogeneity and the correlations among the phenotypic parameters were also investigated. In conclusion, WES is a highly effective and economical genetic diagnostic tool in genetically heterogeneous disease such as CMT.
MUTATIONAL SPECTRUM AND CLINICAL CHARACTERISTICS OF A LARGE COHORT OF GNE MYOPATHY FROM INDIA WITH BEEVOR’S SIGN AS A POTENTIAL CLINICAL MARKER
V. Preethish-Kumar¹, O. Pogoryelova², K. Polavarapu¹, N. Gayathri³, S. Vengalil⁴, J. Hudson⁵, C. Prasad⁶, H. Lochmüller², A. Nalini⁴
¹National Institute of mental Health and Neuro Sciences, Clinical Neurosciences, Bangalore 560029, India
²Institute of Genetic Medicine, John Walton Muscular Dystrophy Research Centre- MRC Centre for Neuromuscular Diseases, Newcastle Upon Tyne, United Kingdom
³National Institute of mental Health and Neuro Sciences, Neuropathology, Bangalore 560029, India
⁴National Institute of mental Health and Neuro Sciences, Neurology, Bangalore 560029, India
⁵Institute of Genetic Medicine, Northern Genetics Service, Newcastle Upon Tyne, United Kingdom
⁶National Institute of mental Health and Neuro Sciences, Neuro Imaging and Interventional Radiology, Bangalore 560029, India

Background: GNE myopathy is an autosomal recessive disease caused by mutations in UDP N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase (GNE) gene. Homozygous 712 (p.M712T) mutation is found in Middle Eastern families, whereas patients of other ethnicities are usually compound heterozygous or homozygous for different mutations.

Objectives: To decipher the most prevalent novel mutations among Indian GNE patients. To describe a new clinical sign in GNE myopathy.

Methods: Direct sequencing done for coding exons 1 to 13 and >10 nucleotides of 5’ and 3’ intronic sequence. Alamut-Mutation software to predict pathogenicity of novel variants. Available patients were examined for presence of Beevor’s sign. Two patients underwent MR Imaging of the abdominal muscles to demonstrate differential involvement of rectus abdominis muscle.

Results: At the time of evaluation the mean duration of illness was 6.6 ± 5.6 years. The mean age at presentation was 32.8 ± 8.5 years and age at onset: 26.2 ± 7.2 years. 42 patients were genetically confirmed [9 homozygous, 33 compound heterozygous and 24 novel mutations] to have GNE myopathy. 33/42 had at least one copy of p.Val727Met mutation in exon 12. Beevor’s sign was observed in 20/22 cases when the hip flexors were of grade 3 or less by MRC grading correlating well with MRI findings.

Conclusion: p.Val727Met mutation is previously described in Middle Eastern Jews, Moslem (Bedouins, Palestinian) and South East Asians. High frequency of this is mutation among Indians is consistent with previous findings. Beevor’s sign in young adult onset non dystrophic distal myopathies could help as a diagnostic clue towards GNE myopathy.
Motor neuronal hyperexcitability potentially contributes to motor neuron death in amyotrophic lateral sclerosis (ALS). Previous studies have reported that ALS motor axons have increased persistent sodium and decreased potassium currents, both of these causing nerve hypereexcitability, and potassium currents decrease with disease progression. While riluzole modulates transient sodium currents in the short-term period, medium-term effects for nerve function have not been proven. Nerve excitability measurements, such as strength-duration time constant (SDTC), recovery cycle and threshold electrotonus (TE), were prospectively performed in 30 ALS patients at baseline and 3 and 6 month later. They commenced riluzole just after initial assessment. At baseline assessment, compared to healthy controls (n = 23), ALS patients had longer SDTC, greater threshold changes in depolarizing TE (TEd), increased refractoriness and increased superexcitability, suggesting increase sodium and decreased potassium currents. Compared to baseline assessment, decreased superexcitability was found at 3 months, and decreased superexcitability and decreased refractoriness and greater threshold changes in TEd were demonstrated at 6 months, indicating decreased potassium currents and blockade of transient sodium currents. Previous studies have reported that superexcitability decreases and TEd increases with disease progression, suggesting increased excitability. Furthermore, riluzole decreases refractoriness and superexcitability in the short-term period, decreased excitability. Disease progression and riluzole alter superexcitability to opposite directions. Decreased superexcitability at 6 months suggests that riluzole partially blocks nerve hyperexcitability for medium-term period. However, riluzole effector site is different from original alterations in ALS, increased persistent sodium and decreased potassium currents. It may results in limited effects for ALS prognosis.
Objective: To evaluate peripheral nerve magnetic resonance diffusion tensor imaging (DTI) as a measure of lower limb disease involvement in amyotrophic lateral sclerosis (ALS).

Methods: DTI was performed on both knees of 23 ALS patients at baseline, 3 months and 6 months. The DTI metrics fractional anisotropy (FA), axial diffusivity (AD) and radial diffusivity (RD) were measured separately for the peroneal and tibial nerves in the popliteal fossa. DTI metrics were correlated with the burden of disability (measured using the ALS functional rating scale, revised – ALSFRS-R), disease duration, lower limb muscle strength, tibialis anterior (TA) motor unit number estimation (MUNE) and TA compound muscle action potential (CMAP) amplitude. MRI data were compared with 13 age-matched controls.

Results: At baseline, peroneal nerve FA was reduced relative to controls (ALS = 0.413+/− 0.011; control = 0.464+/− 0.019; p = 0.03). Other DTI metrics were similar between ALS and control groups. Baseline peroneal nerve FA correlated with ALSFRS-R (rho=0.513, p<0.001), disease duration (rho=-0.356, p=0.02), tibialis anterior MUNE (rho=0.343, p=0.038), and tibialis anterior CMAP amplitude (rho=0.038, p=0.02). Tibial nerve FA correlated with ALSFRS-R (rho=0.749, p=0.0001). There was no significant difference between any measure on serial studies.

Conclusions: FA, a DTI metric associated with axonal loss, was strongly correlated with measures of disability and neurophysiological estimates of motor unit loss in ALS. The lack of change over time may suggest that substantial axon loss occurs in the presymptomatic phase of ALS.
Session 7- Stroke 1
BILATERAL CEREBRAL HEMORRHAGE: DO THEY HAVE BAD PROGNOSIS?

B. Das1,2, D. Khurana1, S. Mehta1, S.R. Bhatkar1, V.Y. Vishnu1, C.K. Ahuja2, V. Lal1
1Postgraduate Institute of Medical Education and Research PGIMER, Department of Neurology, Chandigarh, India
2Teerthanker Mahaveer Medical College and Research Centre, Department of Neurology, Moradabad, India
3Postgraduate Institute of Medical Education and Research PGIMER, Department of Radiology, Chandigarh, India

Objective: Cerebral dual hemorrhages (CDH) are unusual and limited to case reports. Their presence has long been reported as worse prognosis in the limited available literature. However with promising results of newer management strategies for ICH, they may not portend a bad outcome. Hence we aim to address the outcome of CDH patients in a tertiary care hospital in North India.

Patients and Methods: We prospectively looked for CDH in all acute hemorrhagic stroke patients presented in the emergency department of our hospital, from January 2013 to June 2015. In addition to computed tomography of head, baseline investigation like platelet count, coagulogram and cerebral angiography was done to rule out causes of CDH other than hypertension.

Results: During this period we noted six patients of CDH, associated with hypertension. Four patients were over 50 years of age while two were young strokes (43 and 17 years of age) and one was female. Three patients had bilateral basal-ganglia bleed (BBB), one had bilateral thalamic bleed (BTB) while two had dual pathology. All but one were known hypertensives with poor drug compliance. Patients were managed with intensive blood pressure control as per guidelines (INTERACT 2). All but one patient had significant improvement in sensorium at discharge.

Conclusion: CDH in contrast to previous belief, may be associated with better outcomes if managed with aggressive BP control as per current ICH treatment guidelines.
EFFICIENCY OF RAPID RESPONSE TEAM (BRAIN ATTACK TEAM) FOR ACUTE ISCHEMIC STROKE IN A TERTIARY MEDICAL FACILITY AN OPERATIONS MANAGEMENT PAPER

M.K. Flores¹, J.J. Tiongson²

¹The Medical City, Neurology, Quezon City, Philippines
²The Medical City, Neurology, Pasig City, Philippines

Introduction: Treatment of acute ischemic stroke (AIS) involves early IV rTPA and admission at the Acute Stroke Unit. The main barrier in reaching treatment goals in AIS is its relatively short time window; hence, Brain Attack Team (BAT) was conceptualized. This paper aims to describe the BAT process used in a tertiary medical facility.

Methodology: This is a descriptive, operations' management study recounting the BAT process in a tertiary medical facility in the Philippines. 50% from a total of 906 BAT activated from January 2013 to December 2014 were included in the study. These charts were randomized using Random Number Generator. Each chart was coded from 1 to 906 where a total of 453 charts were reviewed. SWOT analysis and process mapping were done to analyze and generate strategies.

Results: 228 were females and 225 were males with a mean age of 59, median of 59, and mode of 60. Most samples fell under the age range of 60-69 and under the NIHSS scores of 0-5. The mean NIHSS was 9, median of 5, and mode of 0. Comparing the AHA/ASA recommended door to needle time, it was noted that door to ER physician evaluation and cranial imaging acquisition were at par or better than what is recommended by AHA/ASA. Other parameters were subpar.

Conclusion: BAT process in the medical institution studied is not efficient whereby 4 areas of delay were identified. Recommendations were identified where improvements were focused on 3 key areas: Workforce, Communication Systems, and External Services.
The relationship between vitamin D deficiency and stroke was cross-sectionally evaluated in the high-risk Asian Indian population. Age- and gender-matched, 239 ischemic stroke patients and 241 control subjects were recruited. Vitamin D status was estimated by measuring serum 25-hydroxyvitamin D (25(OH)D) levels. After multivariate adjustment for a range of potential covariates in a logistic regression model, an inverse association was found between serum 25(OH)D concentration and risk of ischemic stroke: subjects with severely low 25(OH)D levels ($\leq 9.33$ ng ml$^{-1}$) were found to be at 3.13-fold (95% confidence interval (CI), (1.22–8.07)) increased risk of ischemic stroke as compared with those with high levels. Adjustment for systolic blood pressure levels was found to abrogate this association (odds ratio (OR) = 2.00, 95% CI = 0.61–6.50). On stratification, a pronounced association was found between low 25(OH)D and risk of ischemic stroke in hypertensives, OR = 13.54, 95% CI = 1.94–94.43 as compared with no association in non-hypertensives, (Pinteraction = 0.04). We conclude that high blood pressure partly explains the association between 25(OH)D levels and ischemic stroke. Presence of hypertension amply aggravates the risk of ischemic stroke associated with low vitamin D levels. Meticulous management of hypertension, regular monitoring of serum 25(OH)D levels and treatment of severe vitamin D deficiency, particularly in hypertensive subjects, could help in effective prevention of stroke.
ASSOCIATION BETWEEN TUMOR NECROSIS FACTOR-ALPHA (G308A, G488A, C857T AND T1031C) GENE POLYMORPHISMS AND RISK OF ISCHEMIC STROKE IN NORTH INDIAN POPULATION: A CASE-CONTROL STUDY

S. Misra1, P. Kumar1, A. Kumar1, R. Sagar1, K. Prasad1

1All India Institute of Medical Sciences, Department of Neurology, New Delhi, India

Abstract Text

Background: Genetic factors may play a role in the susceptibility of Ischemic stroke (IS). Previous studies have shown that Tumour necrosis factor-α (TNF-α) gene polymorphisms were associated with the risk of IS in multiple ethnicities. The present case-control study tested the hypothesis that genetic polymorphisms of the TNF-α gene may affect the risk of IS in North Indian population.

Methods: Genotyping was determined by using SNaPshot method for 250 IS patients and 250 age- and sex-matched IS free controls. Conditional logistic regression analysis with adjusting multiple demographic and risk factor variables was used to calculate the strength of association between TNF-α gene polymorphisms and risk of IS. Haplotype and Linkage disequilibrium (LD) analysis was done by using Haploview version 4.2 software.

Results: An independent association between TNF-α G488A (OR=2.59; 95% CI 1.46 to 4.60; p=0.001) and C857T (OR=1.77; 95% CI 1.01 to 3.11; p<0.04) and risk of IS was observed under dominant model. However, no significant association between G308A and T1031C gene polymorphisms and risk of IS was observed. Haplotype analysis showed that A308-G488-C857-T1031 haplotypes were significantly associated with the increased risk of IS [OR=1.66; 95% CI 1.02 to 2.71; p=0.003]. Strong linkage disequilibrium (LD) was observed for G488A and C857T (D’=0.41, r²= 0.004).

Conclusions: In North Indian population, two SNPs (G488A and C857T) of TNF-α gene and their haplotypes are significantly associated with the risk of IS. Our findings indicate that polymorphisms and haplotypes of TNF-gene may be used as a genetic marker for identifying individuals at increased risk for developing IS.
PREDICTORS ASSOCIATED WITH POSITIVE D-DIMER RESULTS IN PATIENTS WITH ACUTE STROKE

S. Miyazono\textsuperscript{1}, Y. Tanno\textsuperscript{1}, T. Mori\textsuperscript{1}, T. Iwata\textsuperscript{1}, S. Kasakura\textsuperscript{1}, K. Yoshioka\textsuperscript{1}

\textsuperscript{1}Shonan Kamakura General Hospital, Department of Stroke Treatment - Stroke Center, Kamakura, Japan

【Objective】

Acute stroke patients have an increased risk of venous thrombosis because of immobility. We have measured D-dimer levels on admission to find the patient who had a preexisting venous thrombosis. We investigated the predictive factors of elevated D-dimer level retrospectively.

【Methods】

Included in our analysis were acute stroke patients 1) who were admitted to our institution from Jan.2016 to March.2016, 2) and evaluated for VT with a quantitative D-dimer level on admission.

Evaluated were patient's baseline characteristics, stroke subtype, residence location, mRS before stroke, onset-to-arrival time, NIHSS score, blood test findings on admission. We evaluated the factors associated with positive D-dimer results on admission.

【Results】

102 patients were analyzed. Their average age was 76.8 years. A total of 86(84.3\%) were ischemic stroke patients, 16 (15.7\%) were hemorrhagic stroke patients. Median NIHSS was 3 (1-7: interquartile range), median mRS before stroke was 0(0-3), average BUN levels was 17.9mg/dl, D-dimers were positive in 43(42\%) patients on admission.

Significant positive predictors of D-dimer positive included increasing age, nursing home resident, elevated serum BUN, mRS of 3 or more before stroke. Logistic regression analysis demonstrated that increasing age, elevated serum BUN, mRS>=3 before stroke were the independent predictive factors for D-dimer positive. ROC curve (AUC 0.841) showed that cut-off-point for the BUN level and the age were 15.1mg/dl and 88 years old.

【Conclusion】

Increasing age(>=88 years old), elevated serum BUN (>=15.1mg/dl), mRS >=3 before stroke were associated with positive D-dimer test.
FDG-PET IMAGING OF PLAQUE INFLAMMATION HELPS IN RISK STRATIFICATION AND PROGNOSTICATION IN RECENTLY SYMPTOMATIC CAROTID STENOSIS

V. Sharma\textsuperscript{1}, B. Chandra\textsuperscript{1}, P. Paliwal\textsuperscript{1}, E. Ting\textsuperscript{1}, H.L. Teoh\textsuperscript{1}, B. Chan\textsuperscript{1}, A. Sinha\textsuperscript{1}

\textsuperscript{1}National University of Singapore, Neurology, Singapore, Singapore

Background and aims: Symptomatic carotid stenosis is associated with increased risk of stroke recurrence. Currently, therapeutic decisions are largely based on luminal narrowing, which explains regional hypoperfusion as the underlying mechanism. Plaque inflammation, the initiating event for plaque rupture and thromboembolism (artery-to-artery embolism), is not evaluated routinely in carotid stenosis. Using combined 18F-fluorodeoxyglucose positron-emission tomography (FDG-PET)/computed tomography (CT), we investigated the role of plaque inflammation and stroke recurrence in our cohort of stroke patients with recently symptomatic carotid stenosis.

Methods: This ongoing prospective study aims to include consecutive patients within 30-days of recent stroke and ipsilateral carotid stenosis (≥50%). FDG uptake is quantified as mean standardized uptake values (SUV, g/ml). Patients are followed for stroke recurrence. Embolic potential of the carotid plaque is estimated by presence of spontaneous microembolic signals (MES) on continuous transcranial Doppler monitoring of middle cerebral arteries (MCA) for 40-minutes.

Results: Of the 28 patients included in the study, 6 suffered from recurrent cerebral ischemic event in the same vascular territory within 90-days. In patients with recurrent cerebral ischemia, the mean SUV value in the carotid plaque on the side of symptomatic carotid stenosis was higher (3.46g/ml) as compared to the patients without stroke recurrence (1.72g/ml; \(p=0.03\)). MES were noted in 4/6 cases with recurrent cerebral ischemia as compared to 2/22 asymptomatic cases (\(p=0.001\)).

Conclusions: FDG-PET/CT aids in imaging plaque inflammation in carotid stenosis and identifying high-risk patients. We intend to develop a robust prediction model for risk stratification based on luminal stenosis and plaque characteristics for better therapeutic decision-making.
Background and aims - Neurological fluctuations are frequent during first few days in thrombolysed acute ischemic stroke (AIS) patients. Underlying mechanisms for these fluctuations often remain unclear. Cerebral homeostatic balance is regulated by autoregulation and neurovascular coupling (NVC). We hypothesized that neurovascular uncoupling leads to the clinical fluctuations.

Methods - In this ongoing prospective study, thrombolyzed AIS patients were recruited within 12-hours of symptom-onset. Serial CT perfusion (CTP) imaging (within 12-hours, at 24 and 72-hours) were performed. Serial Quantitative EEG (QEEG) were performed, close to CTP. Alpha band (8-15Hz) power was determined for each hemisphere using 10-seconds epochs. Neurological status was monitored with serial NIH stroke scale (NIHSS) scores. Neurovascular uncoupling was defined as mismatch among CTP, QEEG and clinical findings. Data were analysed independently by investigators blinded to clinical findings.

Results - A total of 32 patients (19 male, median age 68-years (range 56-86) were included. Median NIHSS score was 8-points (range 1-24). NIHSS fluctuations by 4 or more points (deterioration followed by improvement or deterioration following improvement in absence of re-occlusion) was noted in 13 (40%) cases. Increasing cerebral edema (2 cases) and regional hyperperfusion (4 cases) were seen on serial CTP. Remaining 7 cases showed serially improved CTP. QEEG showed significantly increased inter-hemispheric alpha band power ratio (unaffected/affected hemisphere ratio more than 1.5), independent of CTP results, suggestive of neurovascular uncoupling as the underlying mechanism for early neurological fluctuations.

Conclusion - Neurovascular uncoupling is relatively frequent during first few days of AIS. Multi-modal monitoring may help in appropriate therapeutic decision.
ENDOVASCULAR THERAPY FOR ACUTE ISCHEMIC STROKE IN SINGAPORE: A SINGLE CENTER 7-YEAR EXPERIENCE

P. Paliwal¹, L. Yeo¹, C.S.R. Seet², A. Gopinathan¹, J. Vijayan¹, J. Ong¹, A. Chan¹, C. Bharatendu¹, Y.F. Chong¹, C.H. Tan¹, B. Chan¹, M. Nadarajah¹, H.L. Teoh¹, V.K. Sharma²
¹National University Hospital, Medicine, Singapore, Singapore
²National university of Singapore, Medicine, Singapore, Singapore

Background and aim:

There has been a paradigm shift in the treatment approach for acute ischemic stroke (AIS) following the publication of 5 randomized clinical trials for endovascular therapy (ET). However it was widely practiced for stroke patients even before that, especially for patients with posterior circulation stroke and those ineligible for intravenous thrombolysis (IVT). We looked at predictors for favorable functional outcome at 3-months in our AIS cohort.

Methods:

Consecutive AIS patients who underwent ET at our center since 2008 were included. Patients were divided into 2 groups depending on their eligibility according to current AHA guidelines. Information on demographic characteristics, vascular risk factors and time from onset-to-groin puncture (OTT) and CT-to-groin puncture (CGP) were recorded. Recanalization was assessed by modified TICI classification. was Modified Rankin Scale (mRS) score 0-2 at 3-months defined favorable functional outcome (FFO). Safety was assessed by symptomatic intracranial hemorrhage (SICH).

Results:

A total of 69 AIS patients underwent ET during the study period. Median NIHSS was 20 (IQR 17-26). 66% patients received IVT. Mean OTT and CGP were 270 and 147 minutes, respectively. Only 51% patients fulfilled AHA indications for ET. TICI 2b/3 recanalization was achieved in 66%. FFO, SICH and mortality was noted in 33%, 13% and 24%, respectively. Arterial recanalization was independently associated with FFO (OR 6.482, 95%CI 1.436-29.263, p=0.015). Adherence to the AHA guidelines did not affect the outcome measures.

Conclusion:

Current AHA guidelines appear too restrictive and endovascular intervention may be effective in carefully selected AIS patients.
Session 08: Multiple Sclerosis (PACTRIM)+
Stroke 2
Objective: To estimate the prevalence of anti AQP4 antibody in patients with IIDDs presented to UMMC, their clinical and radiological presentation, and prognosis.

Methods: Retrospective review of 102 patients presented with IIDD from 2005 to 2015. Anti AQP4 antibody was tested using the IIFT cell based assay.

Results: Anti AQP4 antibody was detected in 53% of patients. CMS was more common in the seronegative group (57.45% versus 1.89%; p < 0.001). OS involvement and LESCLs on MRI were more common in the seropositive group (49.06% versus 10.64%; p < 0.001, and 72.50% versus 18.92%; p = 0.004, respectively). The relapse rate and EDSS were higher in the seropositive group (5.43 versus 3.17; p = 0.005, and 4.07 versus 2.51; p = 0.006, respectively). Typical clinical presentations that defined NMO were also seen in the seronegative patients.

Conclusion: Our cohort of patients has a higher prevalence of seropositivity of anti AQP4 antibody as compared to the Western countries. This was also associated with a more typical presentation of opticospinal involvement with LESCLs on MRI, higher rate of relapse and EDSS. Nevertheless, there were still overlaps in term of clinical presentation and imaging findings in the AQP4 negative patients.
CLINICAL PROFILE OF PATIENTS WITH ANTERIOR ISCHEMIC OPTIC NEUROPATHY (AION) PRESENTING TO A TERTIARY CARE CENTRE IN NORTH INDIA

INTRODUCTION: Ischemic optic neuropathy is one of the major causes of blindness or seriously impaired vision, especially in older age groups. Non-arteritic AION is the most common form, arteritic form being associated with giant cell arteritis. With the rising prevalence of medical comorbidities in the eastern population now matching the western trends, this entity holds importance as a major cause for vision loss.

OBJECTIVE: To assess the clinical profile of patients presenting with AION in a tertiary care hospital.

MATERIALS AND METHODS: In an observational study from June 2014 to December 2015, all patients presenting with sudden loss of vision were evaluated. Inclusion criteria were disc edema or sectoral pallor on fundus examination, consistent field defect on perimetry and filling defect on fundus fluorescein angiography. All patients underwent routine biochemical investigations along with a detailed ophthalmic evaluation.

RESULTS: 22 patients (24 eyes) have been enrolled in the study. 10 of these were females and 12 males. 7 (29%) had recurrent events. Low Cup: Disc ratio was not significantly associated (p=0.68) with risk of recurrence. 10 (44.4%) had diabetes, 13 (59.1%) hypertension and 9 (40.9%) were smokers. 7(31.8%) patients complained of headache. Of the 11 (45.8%) eyes had visual acuity better than 6/18.

DISCUSSION AND CONCLUSIONS: AION is the most common cause of optic neuropathy in elderly. Diabetes, hypertension and smoking were among the common risk factors associated. Patients presented with normal visual acuity despite the severity of visual field defects.
Multiple Sclerosis (MS) is an autoimmune demyelinating disorder characterized by distinct episodes of neurologic deficits, separated in time, attributable to white matter lesions that are separated in space. This study investigated whether there is a relationship between neutrophil-lymphocyte ratio (NLR) and vitamin D levels to MS severity and if it can be used as a marker of the disease severity, which will help to determine the prognosis of the disease.

We retrospectively enrolled the laboratory results of 60 MS patients and 60 sex and age-matched healthy controls. We found that NLR values of the MS patients were significantly lower than those of the controls. NLR values were also positively correlated with vitamin D levels and red cell distribution width (RDW) and negatively correlated with severity score in MS groups. In conclusion, NLR could be considered as a new inflammatory marker for assessment of inflammation in MS patients with its quick, cheap, easily measurable property with routine complete blood count analysis.
CORRELATES OF MOTOR DISABILITY AND FATIGUE WITH QUANTITATIVE MRI PARAMETERS IN RELAPSING REMITTING MULTIPLE SCLEROSIS AND NEUROMYELITIS OPTICA

L.K. Sreevidya1, M. Netravathi1, R.D. Bharath2, P. SatishChandra1, P.K. Pal1
1National Institute of mental Health and Neuro Sciences, Neurology, Bangalore 560029, India
2National Institute of mental Health and Neuro Sciences, Neuroimaging and Interventional Radiology, Bangalore 560029, India

Background: Relapsing Remitting Multiple sclerosis (MS) and Neuromyelitis optica (NMO) are primary demyelinating disorders with almost similar clinical symptoms but have varied etiology and response to treatment.

Objective: To study and compare clinical (fatigue depression and disability scores), electrophysiological and imaging characteristics of RRMS and NMO.

Methods: 23 RRMS and 14 NMO patients were recruited over a period of 5 years and all parameters were done pre and post steroid therapy.

Results: Mean age at presentation - RRMS-31.1±12.2 years; NMO-34.8±10.9 years. Mean duration of illness- RRMS-50.9±58.1 months; NMO-42.9±48.6 months. Age at onset of illness - RRMS-26.9±10.7 years; NMO-31.9±9.2 years. Frequency of episodes were high in NMO (predominantly myelopathy) as opposed to RRMS (Brainstem syndrome). Disability, fatigue scores and Cerebrospinal fluid pleocytosis were significantly high than MS. Somatosensory Evoked Potentials (EPs) showed significant prolongation in RRMS while Visual EPs showed no difference between both entities. Duration of illness correlated positively with total T1, T2 lesion load and disability scores with T1 lesion load in RRMS. No correlation was found in any clinical scores and lesion load in NMO. As compared to NMO right uncus, insula and anterior cingulate gyrus were relatively preserved in RRMS with atrophy of left pre cuneus, cuneus, occipital gyrus, cerebellum and bilateral pulvinar as identified by voxel based morphometric analysis.

Conclusion: Patients of NMO were of later age at onset with more disability and fatigue compared to RRMS. Duration of illness correlated with total MRI lesion load and disability with T1 lesion load in RRMS.
AOCN-0075
Session 08: Multiple Sclerosis (PACTRIM)+ Stroke 2

COMPARISON OF SIMPLE CBF GRADES BASED ON CT PERFUSION WITH MULTIPHASE CT ANGIOGRAPHY
Y. Tanno1, T. Mori1, T. Iwata1, S. Kasakura1, K. Yoshioka1
1Shonan Kamakura General Hospital, Department of Stroke Treatment-, Kamakura, Japan

【Objective】The aim of this study is to compare CBF grades based on CT perfusion (CTp) with those based on multiphase CTA (mCTA).【Methods】Included in our retrospective analysis were acute stroke patients 1) who were admitted to our institution from August 2012 to June 2015, 2) who were admitted to our hospital within 12 hours of onset and underwent CT angiography showing complete occlusion of the M1 segment of the middle cerebral artery (MCA), or all M2 segments, or the internal carotid artery (ICA) and the M1 segment in the affected side. Evaluated were patient's baseline characteristics, CBF grade of CTp, and types of mCTA. CBF grade was calculated by using bilateral time-density curves (TDCs) of CTp. TDCs were generated on regions of interests set at symmetrical positions of the bilateral MCA territories. According to the time to peak (TTP) and the peak value (PV) comparing the affected side (a) with the contralateral side (c), CBF grade 1 was defined as $TPa - TPc(TTP_{delay}) \geq 2$ second(s) and $PVa/PVc(PV\%) < 0.25$, grade 2 as $TTP_{delay} \geq 2$ s and $0.25 \leq PV\% < 0.75$, grade 3 as $TTP_{delay} < 2$s or $PV\% \geq 0.75$. In addition, poor, moderate or good collateral (pC, mC or gC) was defined according to the ESCAPE trial method.【Results】31 patients were analyzed. Their average age was 73.9 years old. In pC, mC and gC, there were 1, 15 and 15 patients. The one patient of pC had CBF grade 1, the 15 patients of mC were classified to grade 1 in one, grade 2 in 10 (66%) and grade 3 in 4 patients, the 15 patients of gC to grade 2 in 1 and grade 3 in 14 patients (93%).【Conclusion】Our results indicate that pC is probably regarded as our CBF grade 1, mC as grade 2 and gC as grade 3.
ERK/MSC TRANSPLANTATION IMPROVES NEUROLOGICAL FUNCTION BY ENHANCING SURVIVAL OF IMPLANTED CELLS AND MODULATING NEURAL STEM CELLS/NEURAL PROGENITOR CELL PROLIFERATION AND NEUROINFLAMMATION AFTER STROKE IN RATS

Q. Yuan\textsuperscript{1}, X. Qao\textsuperscript{1}, L. Dou\textsuperscript{1}, L. Huang\textsuperscript{1}, J. Zeng\textsuperscript{1}, Y. Zhang\textsuperscript{1}

\textsuperscript{1}Shanghai Tongji hospital- Tongji University School of Medicine- China, Department of Neurology, Shanghai, China

Previous reports have demonstrated the beneficial effects of mesenchymal stem cell (MSC) transplantation in stroke models. The ERK1/2 signal pathway is well-known for cell survival, differentiation and proliferation. In this study, the hypothesis was tested that MSCs stably overexpressing ERK1/2 (ERK/MSCs) might enhance the viability of grafted MSCs after stroke and consequently, exerted better effects. Our results revealed that ERK/MSCs showed better viability in physiological and glutamate-induced neurotoxic condition and more neurons differentiated from ERK/MSCs when neural induction in vitro compared to MSCs (infected with blank virus). After transplantation in rats post stroke, more numbers of grafted cells and improved functional recovery were observed in ERK/MSCs treated rats compared with MSCs treated rats. The ERK/MSCs treated rats significantly increased proliferation of neural stem cells/neural progenitor cells (NSCs/NPCs) in the subventricle zone (SVZ) and neuronal de-differentiation adjacent to the SVZ, enhanced reactive astrocytes but suppressed microglial activation compared with MSCs treated rats. In related to glial activation, elevated TNF-\textalpha levels were found in ERK/MSC treated rats. Taken together, these observations suggest that transplantation of ERK/MSCs improves functional recovery after stroke in rats likely via enhancing survival of implanted cells and modulating the proliferation, neuronal de-differentiation and neuroinflammation. We suggest that transplantation of MSC overexpressing ERK1/2 may be an effective mean for treatment of ischemic stroke.