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Abstracts

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TS1-3

Methods in Neuroepidemiology*Logroscino, G.^{1,2}*

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The lectures will be part of a course focusing on study design and some relevant issues in the epidemiology of the neurological disease (with Dr Rocca). In three lectures I will outline the study design, methods and applied examples of the following topics:

1) Setting of different epidemiologic studies with emphasis on descriptive epidemiology. Descriptive epidemiological studies are better suited to understand key issues on the role of setting in determining results of studies, including analytic studies exploring causal associations.

2) Efficacy vs. effectiveness. Efficacy can be described as the results of an intervention in ideal circumstances while effectiveness explores the results of the same intervention in the real world. Generally efficacy overevaluate the effect of the intervention. The methodologies to outline the differences between the two types of studies will be reviewed. Patient characteristics including compliance, referral system and the relevant decisions of health providers will be considered when assessing effectiveness and its consequence for practice of neurology in recent years.

3) The randomized controlled trial is generally considered at the top of study design in studies in human beings in the pyramid

of scientific evidence. The characteristics that make RCTs similar to basic science research is that the investigator has complete control of the exposure. Participants are assigned to the treatment conditions at random to avoid the effect of possible confounding factors. However the conduction of RCTs in neurological diseases has some specific difficulties and the interpretation of the results are often difficult. Examples of recent advances and failures, especially in the area of neurodegenerative diseases research will be provided.

KS1

Epidemiology, Cohorts and 'Big Science'*Hofman, A.*

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In 2002 Sir Richard Doll wrote, after more than half a century of cohort studies on lung cancer and occupational diseases, that '...cohort studies in the modern sense...have established themselves as essential tools for epidemiological research...and cohort studies have, I suspect, an even more important part to play in the future of medical research than they have had in the past. This presentation will elaborate the crucial role of cohort studies in medicine, amongst others in genome-wide association studies of genes, and in studies of blood biomarkers and imaging characteristics in the etiology and early diagnosis of major diseases, in particular of neurological diseases.

PS1 – Contribution of the GBD to Our Understanding of Neurological Diseases

PS1-1

Global Burden of Mental and Substance Abuse Disorders

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Background: The Global Burden of Disease Study 2013 (GBD 2013) provides the most recent estimates of disease burden and quantified burden for 306 diseases and injuries, across 188 countries, by sex, age, and year. This presentation describes the results from GBD 2013 for the twenty mental and substance use disorders included in GBD 2013.

Methods: Burden was quantified in terms of years lived with disability (YLDs) and years of life lost due to premature mortality (YLLs) representing non-fatal and fatal burden respectively. The sum of these two measures gave disability-adjusted life years (DALYs) as a measure of total burden. The advantages and limitations of these methods in relation to mental and substance use disorders are discussed. Application of GBD 2013 findings for service planning are also demonstrated.

Results: As a group, mental and substance use disorders were the leading cause of disability worldwide, responsible for over 20% of global YLDs. However, limitations were identified particularly in regards to the calculation of YLLs, definition of 'health loss', and availability of data. Despite these limitations, implications of GBD findings are significant, and estimates can be used to project service requirements and identify treatment gaps for mental and substance use disorders.

Conclusion: Updated estimates of burden assist in ensuring that a country's health system is sufficiently aligned to its population health challenges. They allow decision-makers to compare the effects of different mental and substance use disorders to other diseases and injuries, as well as changes in burden across time.

PS2 – Risk Factor Epidemiology and Gene-Environment Interactions

PS2-1

Examining Gene-Environment Interactions in Observational Studies

van der Mei, I.

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Most chronic neurological diseases are caused by a combination of multiple genetic and environmental factors. Rothman's 'Causal Pie Model' provides a useful framework to understand this interplay of aetiological factors. There are important outcomes to be gained by examining gene-environment interactions, including improved population attributable fraction estimates, improved causal inference, better knowledge of mechanisms as well as potentially improved preventive advice. While there has been a substantial increased interest in gene-environmental in the last decade, there are also significant challenges. Interaction is scale dependent and can be assessed on the multiplicative and additive scale, but the methods to examine additive interactions in observational studies are challenging. Many studies are relatively small, particularly when having access to GWAS data, leading to low power and false-negative findings. Also, publication bias of interaction studies is highly likely as interactions are usually not the primary hypothesis and only 'exciting' significant interaction findings are reported out of a range of secondary analyses. The development of consortia for neurological diseases and strict reporting guidelines, allowing gene-environment interaction meta-analyses, are ways to overcome some of the challenging issues, and will hopefully pave the way for highly influential gene-environment interaction work in the future.

PS2-2**Gene-Environment Interactions in Mouse Models of Neurological Disorders**

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Huntington's disease (HD) is a tandem repeat expansion disorder involving psychiatric, cognitive and motor symptoms. In a transgenic mouse model of HD we have shown that expansion of the polyglutamine tract of the mutant huntingtin protein leads to a spatiotemporally specific cascade of molecular, cellular and behavioural abnormalities. We have also demonstrated that environmental enrichment (which enhances sensory stimulation, cognitive activity and physical exercise) can delay onset of the affective, cognitive and motor endophenotypes. Environmental enrichment and physical exercise induce changes in gene expression, which exhibit temporal specificity and regional selectivity. Our results suggest that the timing and duration of these environmental manipulations are critical in terms of their ability to modify gene expression.

Detailed investigations of these HD mice have revealed depression-like behaviours and cognitive deficits (modelling dementia) which precede and motor deficits. The female HD mice demonstrate early affective abnormalities which can be rescued by administration of clinically effective antidepressant drugs as well as increased physical exercise. We have thus been able to investigate these mice as a model of depression and HD, and have discovered various molecular abnormalities.

These findings have been extended to additional environmental factors (including the negative effects of stress), neuroendocrine modulators and animal models of other brain disorders. Together with epidemiological studies and clinical trials, this research is informing the design of ongoing intervention studies for HD. These approaches may also facilitate the development of 'enviromimetics' for a variety of brain disorders known to be modulated by enhanced cognitive activity and physical exercise.

PS2-3**Examining Gene-Environment Interactions Using Twin Studies**

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Gene-environment interaction ($G \times E$) reflects genetic control of sensitivity to the environment. $G \times E$ is likely to be a common and important source of variation for complex neurological traits. Monozygotic (MZ) twins arise after a single ovulation, after the fertilized egg splits, and thus share 100% of their genes. Dizygotic (DZ) twins arise after a double ovulation and share on average 50% of their genes. Given MZ and DZ twins share their pre- and part of their postnatal environment, differences between MZ twins are due to non-shared environmental influences, whereas the extent to which MZ twins are more similar than DZ twins reflects the influence of genetic factors. It is possible to detect $G \times E$ within various study designs; G and E can be either latent (unobserved) variables (e.g., additive genetic variance, shared environment) or measured variables (e.g., *APOE* genotype, age, sex). So far, most $G \times E$ interactions have been identified through hypothesis-driven research involving only few candidate genes. The genomics era together with the development of genome-wide methods for the study of $G \times E$ interactions has excellent potential to greatly expand upon our knowledge and ability to examine $G \times E$ interactions.

PS3 – Cutting Edge Research in Neuroscience

PS3-2**Best Practice for Investigator-Led Clinical Trials – Experience from Neuroscience Trials Australia**

Soulis, T.

Neuroscience Trials, Australia

Investigator-led/initiated trials (IIT) and clinical research contribute greatly to our understanding of specific therapeutic areas, patient groups, clinical practice and treatments.

Unlike commercial trials, there are often constraints associated with the methodology of how such trials are undertaken including the number of resources allocated, budget considerations, project management philosophies, the type of data management employed, the type and frequency of data auditing and the reporting protocols employed.

Neuroscience Trials Australia is routinely contracted to undertake both IITs as well as commercial projects. Both types of projects are undertaken utilising the principles of Good Clinical Practice (GCP).^{1,2,3} NTA employs a risk-based management

approach to both types of projects. Assessment of the risks are defined at the start of each project utilising a quality risk-based assessment monitoring plan including centralized/remote and on-site management scenarios. The basis of all risk assessments is an expertly designed protocol and Case Report Form (CRF).

This presentation will focus on the review of risk-based scenarios for project management of IITs utilizing real-life examples and case studies.

The presentation will cover all aspects of planning for a successful IIT including classification of critical data and managing protocol compliance to ensure a quality data outcome.

¹FDA Guidance: Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring, August 2013

²Transcelerate Biopharma Inc: Position Paper: Risk-Based Monitoring Methodology, 2013

³ICH E6.

PS3-3

Cost Effective Central Monitoring of Clinical Trials

Lindley, R.I.

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There is imbalance in the priorities of monitoring for clinical trials with too much attention paid to the prevention of fraud, and far too little attention paid to careful trial design to reduce the chance of scientific misconduct. Research waste in clinical trials is common due to: small sample sizes (and thus random error); bias (insecure randomization; unblinded assessment of outcome); premature stopping; inappropriate analysis and errors.

Streamlined design not only reduces the temptation to make up data but reduces unintentional error as well. Central identification of patients (e.g. from routine collected data) or central follow-up, also reduces the chance that patients are fabricated. Perversely, privacy data requirements have made it easier to hide trial fraud.

Central data analysis can identify unusual patterns of data, as it is difficult to fabricate data to achieve one statistical outcome without affecting another variable.

Central trial monitoring techniques used in the Heart Protection Study and the Third International Stroke Trial will be presented.

PS5 – Harnessing Environmental and Social Factors to Improve Outcomes

PS5-3

Peer Mentoring as a Method for Improving Community Integration

Hanks, R.

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The objective of this talk is to examine the role of a peer-mentoring program for persons with traumatic brain injury and their significant others with regard to community integration. A randomized controlled trial at a Midwestern rehabilitation hospital in the United States was conducted with 96 persons with traumatic brain injury and 62 significant others/caregivers. Persons with traumatic brain injury and friends/caregivers who knew the person prior to their injury were randomly assigned to a treatment (mentored) or no-treatment (no mentoring) control group immediately prior to discharge from the inpatient rehabilitation unit and were mentored for up to 2 years. A variety of psychosocial measures were examined, including perceived community integration, at the end of the peer mentoring program in order to determine the impact of the mentoring in both the persons with injury and their significant others/caregivers. This presentation will focus on the outcome of this project on these individuals, as well as how this program is now being extended to those with spinal cord injury. Mentoring can be an effective way to benefit mood and healthy coping after TBI, and it can help to prevent maladaptive behaviors such as substance abuse and behavioral dyscontrol in the living situation. The positive benefits to those who mentor will also be discussed, as this is an area of future research that needs to be examined in greater detail.

PS5-4

Addressing Communication Disorders for Productive Community Integration

Togher, L.

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Communication problems following traumatic brain injury (TBI) can contribute to socially inappropriate behaviour causing lost relationships and social isolation. Two treatments can improve the communication of people with TBI with the goal of fostering community integration: (i) social skills training for the person with TBI and (ii) training for communication partners, such as family members and friends to enable them to deal with difficult communication behaviours and facilitate positive communication interactions. While the first of these approaches has received considerable attention, there has been a paucity of studies investigat-

ing the effectiveness of communication partner training. The presentation will provide the findings of a recently completed 3-arm non-randomised clinical trial investigating the effectiveness of partner training for 44 people with severe TBI. A detailed description of the *TBI Express* communication partner training program will be provided, along with an overview of evidence based assessments used in the trial, an outline of the practical resources freely available online and a summary of the findings of the trial. Identifying outcome measures that are sensitive to change and meaningful to participants is a challenge when designing clinical trials of communication interventions. It will be argued that there is considerable benefit to using a combination of quantitative, self-report and qualitative measures. Qualitative and self-report measures provided increased understanding of communication changes perceived by participants, the impact of those changes and the potent 'ingredients' of the training. Therefore, the use of a range of communication outcome measures is recommended to enable the development of communication goals which contribute to engagement in meaningful and relevant everyday activities.

PS6 – Precision in Neuroepidemiology in Hard-to-Reach Settings

PS6-1

Differences in Stroke Rates and Risk Factors among Western and Asian Countries

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From 1990 to 2010, the age-standardized stroke incidence per 100,000 person-years decreased in Japan (from 262 to 192) and South Korea (from 248 to 175). However, the corresponding incidence in China increased (from 348 to 400). The stroke mortality rate were still high in Asians compared to Westerners, and in 2010, the stroke mortality rate in China was the highest among four countries.

Japanese populations have shown higher salt intake and a genetically higher salt susceptibility compared to Westerners, and excessive drinking and the prevalence of aldehyde dehydrogenase deficiency are higher in Japanese than in Westerners. Japanese men's smoking rate is higher than that in Westerners. Fish and soy consumption in Japan is much higher than in Western countries, although fish and soy food consumption in Japan has recently declined. To reduce their risk of stroke, Japanese individuals should reduce their salt intake, eat more fish and soy products, moderate their drinking, and quit smoking.

Nutrient studies in Japan showed that soy and fish consumption helps reduce the incidence of cardiovascular disease (CVD).

In a large-population prospective study, high soy and isoflavone intakes were associated with a reduced cerebral infarction and its mortality in women; this reduction was pronounced in postmenopausal women. A reduced risk of CVD or cerebral infarction was associated with the dietary intakes of fish and omega-3 polyunsaturated fatty acid (PUFA), a lower ratio of serum eicosapentaenoic acid to arachidonic acid, and a high serum omega-3/omega-6 PUFA ratio. Glutamic acid and glycine intakes may be associated with the risk of stroke mortality. Dietary calcium and vitamin D intakes were linked to a reduced risk of arterial stiffness in men.

Asians individuals need to restrict excessive salt intake, moderate their drinking, and avoid or stop smoking.

PS6-2

Stroke Rehabilitation Trials in Low and Middle Income Countries: Are They Feasible?

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More than two-thirds of the stroke occurs in low and middle income countries (LMICs). Most of the LMICs lack basic stroke services, personnel and infrastructure. The cost of effective medical treatments including thrombolysis and endovascular therapy is borne by the patients and the relatives. Stroke rehabilitation is not well developed in most LMICs and patients are discharged back to their home environment when they become medically stable. In the background of this setting it is a difficult task to carry out complex stroke rehabilitation trials in LMICs. However our center over the last few years was able to complete good quality acute multicentred stroke rehabilitation trials.

The best model of stroke rehabilitation is still not known for LMICs. The novel concept of trained caregiver acting as the 'multidisciplinary team' delivering stroke rehabilitation as a cost-efficient model of care can help in creating sustainable and multi-professional rehabilitation systems in these countries, including provision of services to rural population. Hence Family-led Rehabilitation after Stroke in India: Attend Trial was designed to evaluate, a family-led caregiver-delivered home-based rehabilitation intervention compared to usual care as an effective, affordable early supported discharge strategy for those with disabling stroke in India. The ATTEND trial is being done in 14 centers in the country and the results should be available by October 2016 (sample size 1200).

PS8 – Vascular Alzheimer's Disease

PS8-1

The Incidence of Dementia: Age, Sex, and Time

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Objectives: In this invited lecture, I discuss new concepts related to differences between men and women in their experience of dementia or Alzheimer's disease (AD). I focus on risk and protective factors and on time trends.

Methods: This is a narrative review of the literature. First, I introduce the concept of dimorphic neurology and the distinction between sex (biological) and gender (social-cultural). Second, I provide three examples of risk factors related to sex and gender from the literature. Finally, I talk about time trends in incidence.

Results: Apolipoprotein E genotype is equally common in men and women but increases the risk of AD more strongly in women than in men. Apolipoprotein E genotype is a biological factor that we cannot modify directly, but it interacts with sex or gender related factors that may be modified. Low education increases the risk of dementia in both men and women; however, women historically have had less access to education. Education is a social-cultural factor related to gender that may be modified. Finally, bilateral oophorectomy increases the risk of cognitive impairment and dementia. This factor is restricted to women. Bilateral oophorectomy is a surgical practice related to sex that may be modified. A number of studies have suggested that the incidence of dementia and AD has decreased in recent years. The explanation of these trends may involve sex and gender factors.

Conclusions: Consideration of risk and protective factors in men and women separately may accelerate etiologic research for dementia and AD, and may explain in part the declining trend in dementia incidence. In addition, future preventive interventions for dementia should consider both sex and gender factors (Mielke et al., *Clin Epidemiol* 2014; Rocca et al., *Maturitas* 2014).

PS8-2

The Alzheimer Enigma: Epidemiological Studies of the Causes of Dementia

Hofman, A.

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There is a spectacular increase in life expectancy in nearly all countries worldwide. In this presentation I will discuss the counter-side of this phenomenon: the increase in diseases in the elderly. I will address the possible causes of diseases of old age, with an emphasis on dementia, using data from the Rotterdam Study, a prospective follow-up study of 15,000 persons of 45 years or over that is being conducted in a district of the city of Rotterdam, The Netherlands, since 1990. I will argue that aging, as applied to the individual rather than the population, is an empty concept. In my presentation, I will focus on two sets of putative causes of dementia, genetic factors and vascular factors, and their possible interaction. I will discuss the recent avalanche of genes found through genome-wide association studies, and the novel observations on vascular factors through imaging studies, as well as the application of these findings in the study of the etiology, prediction, treatment and prevention of dementia.

PS8-3

Vascular Dementia: A New Approach to Diagnosis

Sachdev, P.

Centre for Healthy Brain Ageing, University of New South Wales, Sydney, Australia

Purpose: Several sets of diagnostic criteria have been published for vascular dementia (VaD) since the 1960s. The continuing ambiguity in VaD definition warrants a critical re-examination.

Methods: Participants at a special symposium of the International Society for Vascular Behavioral and Cognitive Disorders (VASCOD) in 2009 critiqued the current criteria. They drafted a proposal for a new set of criteria, later reviewed through multiple drafts by the group, including additional experts and the members of the Neurocognitive Disorders Work Group of the DSM-5 Task Force.

Results: Cognitive disorders of vascular etiology are a heterogeneous group of disorders with diverse pathologies and clinical manifestations, discussed broadly under the rubric of vascular cognitive disorders (VCD). The continuum of vascular cognitive impairment is recognized by the categories of Mild Vascular Cognitive Disorder, and Vascular Dementia or Major Vascular Cognitive Disorder. Diagnostic thresholds are defined. Clinical and neuroimaging criteria are proposed for establishing vascular etiology. Subtypes of VCD are described, and the frequent co-occurrence of Alzheimer's disease pathology emphasized.

Conclusions: The proposed criteria for VCD provide a coherent approach to the diagnosis of this diverse group of disorders, with a view to stimulating clinical and pathological validation studies. These criteria can be harmonized with the DSM-5 criteria

such that an international consensus on the criteria for VCD may be achieved. Studies are needed to document the reliability and validity of these criteria, and their utility in the field needs to be established.

Reference: Sachdev P, Kalaria R, O'Brien J, Skoog I, Alladi S, Black SE, Blacker D, Blazer DG, Chen C, Chui H, Ganguli M, Jellinger K, Jeste DV, Pasquier F, Paulsen J, Prins N, Rockwood K, Roman G, Scheltens P. Diagnostic Criteria for Vascular Cognitive Disorders: A VASCOG Statement. *Alzheimer Dis Assoc Disord*. 2014 Mar 13. [Epub ahead of print] PMID: 24632990.

Disclosure: The International Society for Vascular Behavioural and Cognitive Disorders (VASCOG) provided support for the conferences from which this work emanated.

PS8-4

Retina: A Window on Microvascular and Neurodegenerative Pathology in the Brain

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The retina provides a unique window to assess subtle subclinical microvascular and neurodegenerative damage non-invasively *in vivo*. Advances in retinal image analysis techniques have enabled the objective and accurate assessment of both qualitative and quantitative retinal abnormalities. As the retina shares many features with the brain, the retina may in particular provide insights into microvascular and neurodegenerative pathology in the brain. There is a growing body of evidence that retinal microvascular abnormalities including retinopathy signs and quantitative markers such as calibers, fractal dimension and tortuosity are associated with age-related vascular pathology in the brain, including both stroke and dementia, and subclinical MRI-defined

markers of cerebral small vessel disease. Apart from retinal microvascular abnormalities, other retinal components such as retinal nerve fiber layer thickness, ganglion cell layer and inner plexiform layer, which may reflect neurodegeneration, are also found in patients with cognitive impairment and dementia. In addition to the application of retinal imaging in elderly populations, it is also being used in childhood providing crucial insights into early-life factors, which may influence late-life susceptibility to brain pathology. This presentation will provide an extensive overview of current literature on retinal imaging in brain pathology.

Acknowledgments: Dr. Ikram is funded by ZonMW (VENI projectno: 91612163), The Netherlands and NMRC/CSA/038/2013, Singapore.

PS8-5

Diabetes and Alzheimer's Disease

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Type 2 Diabetes mellitus (T2D) and dementia are highly prevalent disorders affecting older people. T2D is associated with a nearly 2 fold increased risk of incident dementia and Alzheimers' disease (AD) dementia. Data are emerging that suggest a mechanistic link between the two disorders, opening up the possibility of common therapeutic options. I will present cross-sectional and prospective evidence from in-vivo and post-mortem studies that examine the strength of the associations between T2D, AD pathology and dementia. I will also present data examining the likely pathways linking T2D and dementia, namely cerebrovascular disease and neurodegeneration. An understanding of these pathways, and the underlying mechanisms may lead to development of new therapeutics for dementia in T2d, or dementia overall.

PLS1 – Getting the Diagnosis Right in Movement Disorders

PLS1-1

The Early Diagnosis of Parkinson's: How Precise Can We Be?

Anderson, T.

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An early diagnosis of Parkinson's disease (PD) is critical to targeting yet to be identified disease-modifying treatments before irreversible neuronal loss occurs. Currently the diagnosis of Parkinson's disease (PD) is clinical despite advances in biomarker and genetic research. Pathological changes are well established by the time cardinal motor features – bradykinesia, rest tremor, rigidity – manifest. Recent attention has focused on detection of signatures that permit earlier diagnosis or prediction of PD. Recent reclassification suggestions therefore include terms such as preclinical and prodromal PD. 'Preclinical' implies pathological change without clinical symptoms, and thus only identifiable via robust biomarkers (not yet available). 'Prodromal' indicates presence of features before conventional PD diagnosis is possible.

Some 50% of persons with isolated rapid eye movement sleep behaviour disorder (RBD) will develop PD, or other alpha-synucleinopathy, up to decades later. Hyposmia is present in most PD patients at the time of diagnosis, and anxiety, constipation, genitourinary problems, and even tremor often arise years before motor features. None of these are specific enough, even in combination, to permit a reliable diagnosis or prediction of PD. Thus, particular emphasis is presently placed on identifying robust biomarkers of preclinical and prodromal PD that might be applied in those apparently healthy persons who can be identified as at risk from a symptom profile. Precision in pre-clinical or prodromal diagnosis is on the horizon but still work in progress.

PLS1-3

Does Brain Imaging Actually Improve Diagnostic Precision in Neurodegenerative Disease?

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The differential diagnosis of parkinsonian syndromes remains challenging, especially early in the disease course. However, confidence in the diagnosis is critical for determining prognosis and for selecting appropriate treatment options. While neuroimaging techniques provide detailed information about brain structure and function, their ability to capture additional information that can inform a clinical diagnosis is an open question. Conventional MRI is helpful for excluding symptomatic parkinsonism due to other pathologies, but advanced MRI and PET techniques hold the potential to provide biomarkers that may facilitate differential diagnosis in clinical practice. Here, I will discuss the recent contributions of advanced MRI and PET imaging techniques to diagnose and track parkinsonian syndromes.

PLS1-4

Immunity and Diagnosis in Movement Disorders – When Should I Think About Antibodies?

Mohammad, S.

Neuroimmunology Group, Institute for Neuroscience and Muscle Research, The Kids Research Institute at the Children's Hospital at Westmead, University of Sydney, Westmead, NSW, Australia

Autoimmune movement disorders are important to recognize because they are treatable, and early treatment improves outcomes. This presentation refreshes the phenomenological features that signal a possible autoimmune basis – chorea, stereotypical movements, dystonia, rigidity and myoclonus syndromes such as stiff-person syndrome. Recent paradigms in autoimmune movement disorders including diagnostic guidelines, autoantibody pathogenesis, and therapeutic considerations are discussed in a case-based manner. Some of the disorders discussed are autoimmune encephalitides associated with movement disorders such as N-methyl D-aspartate receptor encephalitis, progressive encephalomyelitis with rigidity and myoclonus associated with glycine receptor and DPPX antibodies and autoimmune basal ganglia encephalitis, the autoimmune movement disorders (non encephalitic) such as opsoclonus-myoclonus-ataxia syndrome and Sydenham chorea, and movement disorders associated with systemic autoimmune disorders.

PLS2 – MS Epidemiology

PLS2-1

The Epidemiology Multiple Sclerosis: Past Achievements and Future Opportunities

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Australia

Multiple sclerosis (MS) is a complex disease where both environmental and genetic factors contribute to pathogenesis. Descriptive epidemiology provided some key epidemiological features, particularly the gradient of increasing MS prevalence with increasing latitude, documented clearly in 1960. In Australia, the negative correlation between ambient ultraviolet radiation levels and MS regional prevalence was very strong. Two other features were that the MS prevalence was higher in regions where childhood infection was more delayed and the female case excess. Analytical epidemiologic investigation was first characterised by either prevalent MS or MS mortality control studies or clinical intervention studies such as the evaluation of corticotropin in 1967. Natural history and family studies were also of importance. Over the past 15 years, the studies have evolved to include incident MS and first demyelination event case control studies, longitudinal studies measuring genotype and repeated environmental measures, carefully designed trials and molecular epidemiological studies. Evidence accumulated on the presence and role of key risk factors including past Epstein-Barr viral infection, low cumulative sun exposure, vitamin D status, ever smoking and HLA-DR15. These, or factors related to them, appear to account for 64% (44% to 91%) of the onset of first clinical demyelinating events in an Australian multi-centre study. Other possible risk factors include reduced exposure to infant siblings in childhood and low parity. Gene-environment studies have been very useful to build up causal inference that candidate environmental factors are likely to be causal. They have also assisted the understanding of mechanisms. In the future, these studies are likely to involve a range of 'omics measures also. Improved statistical modelling incorporating Mendelian randomisation, time-varying covariates and gene network approaches will be important. Mediation analysis, with careful evaluation of how environmental effects are mediated through intermediate factors, will also contribute to the rapidly evolving field of MS epidemiology.

PLS3 – Precision in Epilepsy Research

PLS3-2

Outcomes of Epilepsy Surgery

McIntosh, A.

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Drug-resistant epilepsy is associated with substantial comorbidities and has a major negative impact on quality of life. Current international guidelines recommend that epilepsy surgery be undertaken for suitable candidates, with the aim of resecting the seizure focus and ablating seizures. While the short-term efficacy of epilepsy surgery has been established, the long-term outcomes are less clear as there are relatively few large surgical cohorts with adequate long-term follow-up. Long-term surgical outcome studies have an important role in identifying risk factors for seizure recurrence. The data presented in this session originates from a large (500+) prospectively followed epilepsy surgical cohort with a median of 17 years (IQR 11–23, range 0.7–36 years) regular follow-up. Potential risk factors for post-operative seizure recurrence and issues around long-term outcome studies will be examined. Data such as these are essential for informing selection of surgical candidates, pre-operative counseling, patient decision-making and post-operative management.

PLS3-3

Psychosis in Epilepsy: Role of Antiepileptic Drugs

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Background: There are no agreed definitions or diagnosis criteria for antiepileptic drug induced psychotic disorder (AIPD) in the classification systems of either epileptology or psychiatry. In this study we investigated the clinical spectrum of AIPD in patients with epilepsy who presented with psychotic symptoms.

Methods: We retrospectively reviewed the medical records of all patients with epilepsy who were diagnosed by a neuropsychiatrist as having psychotic disorders in the Department of Neurology at the Royal Melbourne Hospital from January 1993 to June 2015. We retrieved the data of epilepsy/treatment related predictors, psychotic symptoms profile and outcome. Diagnosis of epilepsy was established in accordance to the classification system of the International League Against Epilepsy (ILAE) while that of psychotic disorder was made up according to both DSM-5 and the

proposal on neuropsychiatric disorders in epilepsy by ILAE. Patients with AIPD were compared to those with psychotic disorders unrelated to antiepileptic drugs assessed over the same period (control group). Univariate comparisons were performed and variables with a value of $P < 0.1$ were selected for the multivariate logistic regression analysis.

Results: We evaluated 2,630 in-patients and out-patients with epilepsy and identified 98 (3.7%) with psychotic disorders. Among these 98 patients, 14 (14.3%) were diagnosed to have AIPD. 71.4% in the AIPD group were female compared with 41.7% in the non-drug induced psychosis group ($P < 0.05$). The percentage of temporal lobe epilepsy was higher in AIPD group (71.4% vs. 38.1%, $P < 0.05$). AIPD group had been treated with more previous AEDs before the index episode of psychosis, compared to the control (3.4 ± 2.0 vs. 2.4 ± 1.8 , $P < 0.05$). Current use of levetiracetam was higher in AIPD group (78.6% vs. 20.2%, $P < 0.01$) while use of carbamazepine was higher in the non-drug induced group (21.4% vs. 44.0%, $P < 0.05$). Multivariate logistic regression confirmed four factors associated with AIPD: female gender, temporal lobe epilepsy and use of levetiracetam, and a negative association with carbamazepine. Disorganized behaviors and thinking were more common in AIPD group compared to the non-drug induced group (100% vs. 72.6% and 78.6% vs. 64.3%, respectively $P < 0.05$). The percentage of continuous treatment with antipsychotic drugs was much lower in AIPD group (14.3% vs. 66.7%, respectively: $P < 0.01$). No patients experienced a chronic course in AIPD group while 40.5% did in the non-drug induced group ($P < 0.05$).

Conclusion: One in seven patients with epilepsy who developed psychosis had AIPD. Female gender, temporal lobe epilepsy and current use of levetiracetam were significant predictors of AIPD while carbamazepine had a negative association. Disorganized behaviors and abnormal thinking were predominant symptoms of AIPD. AIPD differed from non-drug induced psychotic disorders in having better outcome.

PLS3-4

Developing Diagnostic Tools for Epilepsy Genetics Study in Rural China

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Purpose: Research and application of findings in epilepsy genetics in rural areas of China are hampered by lack of validated clinical assessment tools for phenotyping at the primary care level, agreed investigation protocols, established logistics and network, and trained personnel. This study aims to overcome these barriers with emphasis on building research infrastructure and capacity.

Methods: People with epilepsy were recruited from rural areas of four provinces (Henan, Hebei, Ningxia, Shanxi). In stage 1, rural primary care physicians performed phenotyping using clinical assessment tools (questionnaires). Patients then attended the provincial hospitals for independent phenotyping by neurologist assessment, EEG and brain MRI. In stage 2, patients underwent phenotyping by rural physicians and provincial neurologists only.

Blood samples were collected from patients in both stages for DNA extraction and subsequent genotyping. To develop locally valid clinical assessment tools, reference was made to screening questionnaires previously employed for seizure classification, and provincial neurologists were consulted. Their feasibility was pilot tested in the rural areas. Common EEG and brain MRI protocols were checked for compatibility with local equipment and practice.

Results: After piloting testing and revision, clinical assessment tools covering epilepsy history and seizure semiology were developed. Common EEG and brain MRI protocols were employed in the provincial hospitals. Provincial neurologists and rural physicians were trained in clinical and research skills and ethics. A total of 637 patients (625 with evaluable datasets) in stage 1 and 1,435 (1,401 with evaluable datasets) in stage 2 were recruited. In stage 1, among these 625 patients, 262 (41.9%) were female. Their median age at recruitment was 38 years (interquartile range [IQR] 26 to 48). Among patients with one seizure type ($n = 576$), unweighted Cohen's Kappa in seizure classification between rural physicians and provincial neurologists was 0.63. In stage 2, 618 (44.1%) patients were female. Their median age at recruitment was 40 years (IQR 28 to 51); 110 (7.9%) were less than 18 years old. Among patients with one seizure type ($n = 1,378$), unweighted Cohen's Kappa in seizure classification between rural physicians and provincial neurologists was 0.62. These results suggest 'fair to good' agreement in seizure classification between the rural physicians and provincial neurologists in both stages. The phenotype data will be evaluated an expert panel to derive a higher level of seizure classification, based on the clinical description, and EEG and MRI results. Seizure classification by the rural physicians and provincial neurologists will be correlated with that by the expert panel. Further analysis of the phenotype data aims to develop algorithms for classifying seizures based on the seizure classification questionnaires.

Conclusion: An infrastructure system to conduct epilepsy genetics research in rural China has been successfully established through this project. The model developed has the potential to be applied in other low- and middle-income settings where the majority of the world's people with epilepsy live.

PLS4 – Focusing Rehabilitation on the Person and Family in Context

PLS4-1

Family Matters: How Families Living with Disability Perceive and Apply Their Resources to Achieve a Sense of Wellbeing

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Objective: A key issue for family outcomes research is a more situated understanding of the resources of families living with disability and their access to opportunities to promote well-being. The objective of this exploratory study was to develop a conceptual understanding of social and financial resources of families living with disability and how these might relate to their capabilities to function in a meaningful way. A secondary objective was to identify preliminary measures and study design for longitudinal research.

Method: An exploratory case study design incorporating mixed methods was employed. The Capabilities framework (Sen, 1985) was used to conceptualise family resources as a unique set of capabilities that enable or constrain the meaningful functioning of families. As an initial developmental step, four diverse families living with a family member with acquired brain injury (ABI) in south east Queensland were purposively recruited. Each family case study involved three phases of data collection: 1) a family interview; 2) recording of time use by one nominated family member; and 3) a follow-up interview with the nominated family member. All data were combined for a within- and across-case analysis.

Findings: The focus of this presentation is the within-case analysis which derived family specific profiles. The findings describe in a preliminary way conceptual detail of family resources and the link to function and wellbeing, and elucidate issues for future study design. The themes and sub-themes of each family analysis reveal the distinct nature of their wellbeing story and its resource components and how these might be interpreted in terms of family specific capabilities and valued functions.

Conclusion: The study raises interesting theoretical and empirical questions about stability and instability of capabilities of families living with disability and how these shape family wellbeing overtime through the opportunities and compromises produced and how families manage these.

PLS4-2

Family Resilience: An Important Resource for Long-Term Functioning

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Resilience has been identified as a potential factor contributing to the individual adjustment of family members as well as the sustainability of providing longer-term family support to relatives with a traumatic brain injury (TBI) or spinal cord injury (SCI). However, there has been little research on the topic within rehabilitation. Historically, resilience was understood to be an underlying personality trait that people either had or didn't have. Contemporary formulations suggest that resilience is a more dynamic quality, and may encompass a set of skills that can be acquired in the face of adversity. We have been conducting a series of studies among families supporting relatives with traumatic injury (TBI and SCI) to better understand the potential role of resilience.

Our initial studies identified a relationship between resilience and increased family member wellbeing as well as reduced levels of negative affect carer burden. Therefore, it was important to investigate whether family members who reported higher resilience approached the provision of support differently. Results from an ongoing multicentre study found that family members with moderate to high resilience scores on the Resilience Scale ($n = 80$, HRS) were significantly less likely to use escape avoidance ways of coping and more likely to use problem solving (both $p < 0.001$) than families with lower resilience scores ($n = 59$, LRS). There was also a trend for the families reporting HRS to use distancing, confrontive coping and seeking social support more frequently than families reporting LRS ($p < 0.05$). Overall, the families reporting HRS were significantly more likely to employ a Problem-Focused approach ($p < 0.001$) rather than Emotional-Focused coping approaches (ns).

These studies provide a platform for trialling a new psycho-educational program, Strength 2 Strength, which aims to build resilience among families supporting relatives with traumatic injury. Two feasibility studies have reported positive effects from delivery of the program, paving the way for a larger trial in the future.

PLS4-3**The Long-Term Experiences of Stroke Family Caregivers: How Can Technology Promote Improved Relationships?***Ryan, T.*

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There are almost 400,000 people living with the impact of stroke in Australia and over eight million people living with the effects of stroke in Europe, including 1.2 million people in the UK. Emphasis on long term support in the community has become a central feature of policy in recent years and with shortening hospital length of hospital stay, family caregivers are playing an ever more important role, for a longer period of time. The long-term experience of stroke caregivers is relatively under-researched, although thus far it is safe to assume that burden and poor quality of life are central to the experience. This paper will explore the experience of stroke family caregivers from a qualitative study undertaken in the UK and Australia. Twenty-two stroke caregivers participated in four focus groups with the aim of investigating the caregiver role and how service provision is experienced. Major themes of 'becoming disconnected' and 'rebuilding selves' are explored. Furthermore, the paper will investigate the ways in which ICT might be used to begin to address these shortcomings and augment efforts to make connections. In particular the ways in which stroke caregivers might use ICT in their endeavours to maintain relationships, with both formal and informal communities, will be explored.

PLS4-4**Individual and Family Experiences of Pathways, Outcomes and Choice after MVA Acquired sTBI Under Fault-Based and No-Fault Injury Insurance***Harrington, R.^{1,2}; Foster, M.^{1,2}; Fleming, J.³*¹Centre for National Research on Disability, Griffith University, Meadowbrook, Australia; ²School of Nursing, Midwifery and Social Work, The University of Queensland, Brisbane, Australia;³School of Health and Rehabilitation Sciences, The University of Queensland, Brisbane, Australia

Primary Objective: To investigate individual and family experiences of pathways, outcomes and choice after motor vehicle accident (MVA) acquired severe traumatic brain injury (sTBI) under different injury insurance contexts.

Methods: Semi-structured interviews with 10 adults with sTBI and 17 family members explored experiences of pathways, outcomes and choice, under Queensland's, privately underwritten, fault-based compulsory third party (CTP) insurance scheme and Victoria's government run, no-fault transport accident scheme. Participants were sampled to provide variation in injury severity, time post injury, compensable status and regional vs. metropolitan residency. Interviews were thematically analysed to identify dominant themes under each scheme.

Results: Participants engaged with a no-fault scheme generally experienced a sense of security due to a surety of support and more informed access to a rehabilitation focused pathway that also took account of personal choice. The experiences of participants under a fault based scheme contrasted sharply with this finding. The general experience of a fault based scheme was of uncertainty of pathways and pressured lives. This was associated with experiences of rationed resources and unknown choices.

Conclusions: This study provides valuable insights into the experiences of people with MVA acquired sTBI and their families under differing insurance contexts. Findings highlight the potential benefits of no-fault reforms to existing accident and injury insurance schemes.

Topic 01. Prevention

1231

High Sensitivity Cardiac Troponin T (hs-cTnT) Changes in Acute Ischemic Stroke with Rheumatic Heart Disease in China

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Background and Objective: The high sensitivity cardiac troponin T (hs-cTnT) is frequently elevated in acute ischemic stroke (AIS) patients. However, the relationship between the hs-cTnT level and AIS patients with rheumatic heart disease (RHD) remains unclear. We aimed to investigate the characteristics of the hs-cTnT serum level and its influence on outcomes of AIS patients with RHD in China, defined as mortality, poor outcome (disability/mortality), hemorrhagic transformation (HT) and recurrence of stroke.

Method: We retrospectively included AIS patients with RHD who were admitted within 1 month of stroke onset in West China hospital from October 2011 to February 2014. Hs-cTnT level on admission were investigated. Basic characteristics, functional outcomes, HT and recurrence of stroke were compared between an elevated hs-cTnT group (≥ 14 ng/l) and a normal hs-cTnT group (< 14 ng/l).

Results: Of the 84 cases finally included, 58.3% patients had hs-cTnT levels above the reference ($N \geq 14$ ng/l). Patients with elevated hs-TnT had a higher prevalence of hypertension and renal impairment (all $P = 0.024$). Compared to the patients with normal hs-TnT level, those with elevated hs-TnT level showed a significantly higher 3-month mortality, 3-month poor outcomes (disability/mortality), and risk of HT (all $P \leq 0.029$). After adjustment for age, sex, and National Institutes of Health Stroke Scale (NIHSS) on admission, the risk of HT in elevated hs-TnT group was a 3.0-fold higher, and the 3-month death risk was a 5.0-fold higher than normal hs-TnT group.

Conclusion: Renal impairment was independently associated with the level of hs-cTnT elevation in AIS patients with RHD. Hs-cTnT elevation seemed to be related to HT and 3-month mortality closely.

1237

Population Attributable Fractions and Joint Effects of Key Risk Factors for Multiple Sclerosis

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Aim: We examined the combined effect of having multiple key risk factors and the interactions between the key risk factors of multiple sclerosis (MS).

Methods: Data was used from the Ausimmune study, an incident case-control study including cases with a first clinical diagnosis of central nervous system demyelination (FCD) and population-based controls. We used data on: HLA-DR15 (rs9271366), history of IM (no, yes), EBNA IgG (0–40, 160–2560), ever smoked (no, yes), actinic damage (grade 4–6, 1–2 as a measure of lifetime sun exposure), serum 25-hydroxyvitamin D (25(OH)D) level (> 50 , ≤ 50 nmol/l).

Results: Every additional risk factor roughly doubled the odds of disease: compared to those without any risk factors, those with 1, 2, 3, and 4 or 5 risk factors had an increased odds of being a FCD case of 2.12 (95% confidence interval 1.11–4.03), 4.31 (2.24–8.31), 7.96 (3.84–16.49), and 21.24 (5.48–82.40), respectively. Only HLA-DR15 and history of infectious mononucleosis interacted significantly on the additive scale (Synergy Index, 3.78; $p = 0.03$). The five key risk factors jointly accounted for 63.8% of FCD onset. Examining each factor separately, we found that HLA-DR15 contributed most (45.6%), followed by smoking (40.8%) and low actinic damage (30.8%). High anti-EBNA IgG was another important contributor.

Conclusions: A high proportion of FCD onset can be explained by the currently known risk factors, with HLA-DR15, ever smoking and low cumulative sun exposure explaining most. We identified a significant interaction between HLA-DR15 and history of IM in predicting a first clinical diagnosis of CNS demyelination, which together with previous observations suggests that this is a true interaction.

1238

Stressful Life Events and the Risk of Initial CNS Demyelination

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Objective: To examine the association between stressful life events and risk of CNS demyelination, many of whom go on to develop MS.

Methods: This was a multicentre incident case-control study. Cases (n = 216) were aged 18–59 years with a first demyelinating event (FDE) and resident within one of four Australian centres (from latitudes 27°S to 43°S), from November 1, 2003, to December 31, 2006. Controls (n = 395) were matched to cases on age, sex, and study region, without CNS demyelination. Significant life events in the 12 months prior interview were measured using a modified questionnaire based on the Social Readjustment Rating Scale detailing different life events and converted into a stress number and a stress load by using weights of each event.

Results: Compared to those who did not experience any significant life events in the previous 12 months, those who suffered from a serious illness were more likely to have a FDE (OR 2.56 CI: (1.44, 4.55) p = 0.001). However, we did not observe differences between cases and controls for the total number of stressful life events or the total load of stressful life events.

Conclusion: We did not confirm that the total number and load of stressful life events in the twelve months prior to interview increased the risk of CNS demyelination. However, cases were more likely to report a serious illness which could suggest that a non-specific serious illness provides an additional strain to an already challenged immune system.

1279

Higher Intake of Omega-3 Polyunsaturated Fatty Acids Is Associated with a Decreased Risk of a First Clinical Diagnosis of Central Nervous System Demyelination: Results from the Ausimmune Study

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Background: There is contradictory evidence for a role of dietary fat in risk of multiple sclerosis (MS). Objectives: To examine the association between usual fat intake (total, saturated, monounsaturated (MUFA), polyunsaturated (PUFA), omega-3 and omega-6) and risk of a first clinical diagnosis of CNS demyelination (FCD).

Methods: Multicentre incident case-control study in Australia during 2003–2006. Cases were aged 18–59 years and had a FCD; controls were matched to a case on age, sex, and location. Dietary data were collected using a validated food frequency questionnaire.

Results: In 267 cases and 517 controls with dietary data, higher intake (per g/day) of omega-3 PUFA (Adjusted odds ratio, AOR = 0.61 (95% CI 0.40–0.93)), and particularly that derived from fish (AOR = 0.53 (95% CI 0.31–0.93)) rather than from plants (AOR = 0.74 (95% CI 0.39–1.43)) was associated with a decreased risk of FCD. Total fat intake and intake of other types of fat were not associated with FCD risk.

Conclusions: There was a significant decrease in FCD risk with higher intake of omega-3 PUFA, particularly that originating from fish. There was no evidence to indicate that the intake of other types of dietary fat or fat quantity in the previous 12 months was associated with an altered risk of FCD.

1300

The Stroke Riskometer: Reducing the Burden of Stroke Using Mobile Technology (RIBURST)

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Objectives: Strokes are a major cause of death and disability worldwide despite about 80% of strokes being preventable. However, there is low awareness in the population about stroke and associated risk factors, and no widely accessible and simple means to calculate individual stroke risk and motivate people to control their risk factors.

Methods: To address these issues, the Stroke Riskometer mobile app was developed. Users answer a series of questions based on a validated algorithm², which allows them to calculate their 5 year and 10 year risk of stroke, identify the factors that contributed to their risk and calculate their relative risk. The app has built-in research capability, allowing data from the Stroke Riskometer to be collected at baseline and one year follow-up for research (Reducing the burden of stroke using mobile technology, RIBURST) from users worldwide who consent to the study.

Results: To date, over 1300 people have consented to participate in RIBURST (53% from NZ, 25% from UK and USA). As the updated app was launched in March 2015, preliminary results of descriptive analyses of stroke prevalence by demographic groups from data collected over 5 months and plans for future analyses on cohort data will be presented.

Conclusions: The use of the Stroke Riskometer app has the potential to reduce stroke burden worldwide by increasing awareness of individual risk, motivating people to control their risk factors and by providing knowledge and awareness of stroke to the community. The RIBURST study is uniquely placed to collect data international data on stroke and its risk factors particularly from developing countries where such data are sparse.

Effectiveness of an Intervention to Improve Medication Knowledge and Adherence in Survivors of Stroke: A Randomised Controlled Trial

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Objectives: To investigate the effectiveness of a comprehensive, coordinated and individualised program designed to improve knowledge and enhance adherence to recommended secondary prevention therapies in patients with stroke or transient ischaemic attack.

Methods: Shared Team Approach between Nurses and Doctors For Improved Risk Factor Management (STANDFIRM) trial, an on-going prospective, multicentre, cluster-randomised controlled trial, with blinded outcome assessments. Patients aged 18 years or older, who were hospitalised for stroke or transient ischaemic attack were included. Patients were excluded if they were recruited to another trial, or admitted from or discharged into a nursing home. The intervention comprised a comprehensive, team-based, individualised stroke prevention management program, including a nurse-led education and support component, and regular specialist and general practitioner review of care plans. Primary outcomes for this sub-study: patients' adherence to prescribed medications, and knowledge of their medications. Outcome assessments are undertaken at 1 year and 2 years after baseline, using validated nurse-administered questionnaires. The effect of the intervention on medication knowledge and adherence, including the 95% confidence intervals, will be estimated using linear and logistic regression models.

Results: Between January 2010 and November 2013, we recruited 563 patients for the trial. The median age was 70 years (IQR 70), 65% were male, 77% ischaemic stroke, 19% intracerebral haemorrhage, and 14% TIA. Data lock will occur in October 2015.

Conclusions: Findings from this study could help ascertain the importance of interdisciplinary care in implementing strategies to empower survivors of stroke with the knowledge required to optimize medication management, and to ensure long term adherence to recommended secondary prevention therapies.

Does NIHSS Score Predict Acute In-Hospital Complications in Patients with Posterior Circulation Strokes?

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Background: The National Institutes of Health Stroke Scale (NIHSS) is widely used as a standard instrument to evaluate stroke severity and final outcome after a stroke in terms of length of stay, survival, and discharge destination. It is still unclear whether baseline NIHSS score at admission can also predict in-hospital neurological and medical complications (NMC), especially in patients with posterior circulation (PC) strokes.

Aim: To determine whether NIHSS score was associated with in-hospital NMC in patients with PC strokes.

Methods: This prospective study included all patients of PC strokes admitted in a tertiary care centre in India over a one year period (n = 100). NMC included neurological deterioration (ie, worsening by 4 points or more of the NIHSS score during the hospital stay) and all other medical complications that the patients developed during their hospital stay prior to their discharge/in-hospital mortality.

Results: 30.3% of patients with ischemic and 54.2% of patients with hemorrhagic stroke developed NMC. Patients who experienced NMC had higher mean baseline NIHSS score for ischemic (6.4 vs. 4.2, $P < 0.01$) as well as for hemorrhagic stroke (17.1 vs. 12.1, $P < 0.01$). Using receiver-operating characteristic curve analysis, it was found that NIHSS >4 for ischemic stroke was associated with NMC, however, a cut-off value for hemorrhagic stroke could not be established. Also, patients having diabetes ($p = 0.02$) and cardioembolism ($p = 0.04$) as the stroke mechanism had significantly higher risk of NMC.

Conclusion: In posterior circulation stroke patients, increased baseline NIHSS score at admission was associated with an increased risk of in-hospital neurological and medical complications. This association applied to ischemic as well as hemorrhagic strokes. The clinical significance of these findings requires further evaluation in larger prospective studies.

Topic 02. Diagnosis

935

Adolescent Inhalant Abuse: The Use of Growth as a Potential Diagnostic Measure

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Objectives: The abuse of inhalants (e.g. petrol or glue) containing the volatile solvent toluene is a significant public health issue in Australia, especially for adolescent populations, where inhalants are the first drug abused. Inhalant abuse is also a significant health issue in Indigenous communities, with abuse rates up to 60% in some remote settings. Inhalant abuse can lead to chronic health issues including cognitive deficits and metabolic disturbances, and is often a pathway to further drug use. However, the identification of at-risk individuals is difficult and diagnostic tools are limited. Our objective was to identify the effects of adolescent inhalant abuse on growth parameters and determine whether these may be appropriate clinical measures to improve the identification of adolescents who abuse inhalants.

Methods: We retrospectively analysed haematological, growth, and drug use data from 118 Indigenous males from two remote communities, 86 of whom chronically sniffed petrol as adolescents.

Results: Petrol sniffing was the earliest drug used (mean age 13 years) and was significantly associated with increased likelihood and earlier use of other drugs. Petrol sniffing impaired height ($p = 0.000$) and weight ($p = 0.001$) and was associated with meeting 'failure to thrive' criteria ($p = 0.022$). Duration of petrol sniffing was correlated to reduced height percentile ($p = 0.024$). Growth parameters exceeded the predictive power of serum toluene and other haematological indices as diagnostic tools for inhalant abuse.

Conclusions: Our data indicates that adolescent inhalant abuse is associated with decreased growth and should be included in the differential diagnoses for 'failure to thrive'. Thus growth parameters may represent improved diagnostic models for detecting inhalant abuse, at least in males. The addition of impaired growth to inhalant abuse warning signs may; improve early diagnosis, reduce long-term consequences, and provide a meaningful health promotion message to adolescent males.

1307

Unusual Clinical and Radiological Manifestations of Pediatric Moyamoya Disease: Findings from a Study of 25 Children from India

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Introduction: Presentation of pediatric moyamoya disease, a vaso-occlusive disease, varies significantly as compared to adults. As the treatment outcome depends on neurological status at the time of diagnosis rather than age, early diagnosis of myriad manifestations is the key to good prognosis.

Methods: 25 children of moyamoya disease diagnosed by MRI, MRAngiography/DSA were enrolled; secondary causes ruled out; Various clinico-radiological manifestations were studied.

Results: Mean age: 6.71 yrs (6 months – 15 years); F:M ratio 1.15:1.

Clinically – headache, cognitive decline, visual loss, bihemispherical TIAs, TIA – paraparesis with dysarthria and Radiologically – Boomerang sign, unilateral ICA affection and posterior circulation involvement were the unusual presentations found in this study.

Conclusions: For neurologists, it's important to be familiar with the usual and unusual clinic-radiological manifestations of pediatric moyamoya disease to make an early diagnosis leading to a favorable prognosis of this potentially treatable entity.

Table 1. Unusual manifestations (for Abstract 1307)

Clinical features frequency as presenting feature

- Recurrent TIAs 14 (56%) 2 (8%)
- Headache 12 (48%) 2 (8%)
- Seizures 8 (32%) 1 (4%)
- Cognitive Decline 2 (8%) 1 (4%)
- Bihemispherical TIA 2 (8%) 1 (4%)
- Visual Loss 1 (4%) 1 (4%)
- TIA – Paraparesis with Dysarthria 1 (4%) 0 (0%)
- Hemiparesis 20 (80%) 17 (68%)
- Recurrent stroke 12 (48%)

Table 2. Radiological findings MRI brain (for Abstract 1307)

- A. Ischemic stroke 19 (76%)
 - Anterior circulation strokes 16 (64%)
 - Posterior circulation strokes 2 (8%)
 - Anterior + Posterior circulation strokes 1 (4%)
 - B. Hemorrhagic stroke 1 (4%)
 - C. Normal parenchyma (only abnormal flow voids) 5 (20%)
- Angiography
- Unilateral ICA involvement 4 (16%)
 - Bilateral ICA with normal Posterior Circulation(PC) 18 (72%)
 - Bilateral ICA with PC involvement 3 (12%)
 - Isolated PC involvement 0
 - BOOMERANG SIGN 1 (4%) (Isolated corpus callosal (splenial) infarct)

Topic 03. Epidemiology

1056

Time and Geographical Patterns of Myotrophic Lateral Sclerosis Incidence in the ALS Register, Swabia

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Background: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease with rapid progression and largely unknown etiology. Our aim was to investigate time and geographical patterns of ALS incidence in Southern Germany.

Methods: Since October 2010, all ALS-patients in the catchment area of 8.4 million inhabitants are recorded prospectively in the ALS registry Swabia. Data between October 2008 and September 2010 were collected retrospectively (N = 470 cases), afterwards prospectively. Crude and age standardized incidence rates (ESR) with 95% confidence intervals (CI) were calculated employing direct standardization by 5 year age groups and sex. Average population statistics and the European Standard Population (2013) were applied. Incidence rates were appraised over time and by spatial characteristics.

Results: Until February 2015, 1166 ALS cases (mean age at onset 66.9 (SD 11.9) years, 56% men) were registered of which 1097 cases were included for analysis. Total men-women ratio was 1.25–1. The incidence peaked at the age group 75–79 years. Overall, the crude incidence was 2.19 and the ESR was 2.22 per 100,000 person-years. The highest incidence was observed at the Lake of Constance (crude 3.85, ESR 3.97), lowest in Main-Tauber-Kreis (crude 0.99, ESR 0.93). In urban areas, the incidence was higher (crude 2.25, ESR 2.29 with 95% CI [2.14, 2.44]) than in rural areas (crude 1.95, ESR 1.98 with 95% CI [1.71, 2.24]) but the difference not statistically significant.

Conclusion: ALS incidence varied in the counties, whereby differences in reporting cannot be ruled out. For the prospective part, the ESR was in the range of other European countries and our own retrospective data, confirming 81% completeness as found for the retrospective part by the capture recapture method.

1090

Warning: Stroke as an Emerging Disease of the Young and They Miss the Chance for Acute Therapy

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Objectives: Many studies from the UK and the USA reveal that the average age of stroke patients is falling and that many patients get to the hospital too late for acute treatments. Give that stroke is one of the major causes of death and permanent disability, it is important for us to understand if the same is true in Australia.

Methods: Our retrospective study included patients who were admitted to the Stroke Unit of the Royal Brisbane Women's Hospital, between 2002 and 2011. We analyzed the patient data on the basis of age range (0–10, 11–20, etc.) and year of admission (2002–2006 or 2007–2011).

Results: Preliminary analysis of data from 1993 patients reveal that stroke patients admitted from 2002 to 2006 had a mean age of 69.2 and those from 2007 to 2011 of 65.4. Hence, stroke patients are on average, four years younger than during the previous 5 years ($t(1991) = 5.128, p < 0.001$). All age ranges have seen an increase in the rate of stroke, (+15.24% in working age <65) except ages >70 where the incidence has dropped considerably. Even more of a worry is the fact that young people seem to get to the hospital later than older ones, missing the chance for acute therapy.

Conclusions: As a word of caution, the results have yet to be adjusted for catchment area changes, new stroke units opening, and changes in population statistics. Nonetheless, our study suggests that stroke is becoming more frequent in younger Australians. Primary and secondary prevention techniques are effective, as results from older shows, but that they need to be carried over to younger at-risk groups too, together with an awareness campaign.

1097

High Prevalence of Stroke and Poor Hypertension Control Among Stroke Survivors: A Community-Based Study in Rural Gadchiroli, India

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Objectives: With epidemiological transition the burden of stroke is projected to increase in the developing countries, including India. However, data on the prevalence of stroke in rural India is scarce and in the last 20 years there has been no population-based prevalence study conducted in rural India. In this study we evaluated the prevalence of stroke and hypertension control among stroke survivors in a demographic surveillance site in one of the most underdeveloped districts of India.

Methods: Trained surveyors conducted a house-to-house survey using a validated screening questionnaire in a well defined

population of 45053 living in 39 villages in Gadchiroli district. A trained physician and a neurologist evaluated screen positive patients and diagnosed stroke using the World Health Organization's criteria.

Results: In the screened population, 175 patients had stroke. The mean age of patients with stroke was 60.9. A 14.7 years and 32.5% were women. The crude prevalence rate of stroke was 388.4 (95% confidence interval, 335.04–450.33) and the age-standardized prevalence rate of stroke was 535.58 (95% confidence interval, 492.41–583.01) per 100000 population. The crude prevalence rate of stroke was more than double among men than women (520 vs. 255 100000 population, $p < 0.05$). Hypertension was present in 105 (60%) stroke patients but was adequately controlled in only 31 (29.52%) patients.

Conclusion: The prevalence rate of stroke in this community is more than twice the prevalence rate reported from previous studies in rural India and is higher than the prevalence reported from the low and middle income countries. Stroke is emerging as a public health priority in rural India and risk factor control measures are needed to reduce the preventable morbidity and mortality due to stroke.

1232

Life Expectancy after Traumatic Brain Injury

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Objectives: Determine the mortality, life expectancy, risk factors and causes of death after traumatic brain injury (TBI).

Methods: Three studies were completed. Study 1 included 1,678 adults with TBI admitted to a single rehabilitation facility in the U.S. between 1961 and 2002. Study 2 included 18,998 residents of the U.S. state of Colorado with TBI discharged from acute hospitalization between 1998 and 2003. Study 3 included 6,913 adults with TBI completing inpatient rehabilitation in the U.S. between 2001 and 2010.

Results: Across the 3 cohorts, participants were between 1.5 and 2.5 times more likely to die compared to the general population, with a life expectancy reduction between 4 and 9 years. Identified risk factors for death were older age, being male, previously married, less education, not employed, longer hospitalization, injury severity, metropolitan residence, fall-related TBI, more comorbidities, not discharged home after rehabilitation, less functional independence, and greater disability. Participants were at greatest risk of death due to aspiration pneumonia, seizures, mental/behavioral and neurologic conditions, sepsis, other respiratory conditions, and external causes of injury and poisonings.

Conclusions: There is an increased risk of death for individuals with TBI requiring hospitalization or rehabilitation. Risk factors and causes of death have been identified that may be amenable to intervention.

1233

Changes in Quality of Life after Stroke in the North East Melbourne Stroke Incidence Study

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Objective: Understanding changes in quality of life (QoL) after stroke could provide insights into how to improve the lives of survivors of stroke; however, few longitudinal studies of these survivors exist. We aimed to examine changes in QoL to 10 years after stroke and to assess whether QoL differed by age or sex.

Methods: First-ever strokes ascertained in a population-based stroke incidence study from 1997–99 were followed up at 2, 5, 7 and 10 years after stroke. QoL was assessed with the Assessment of Quality of Life (AQoL) instrument a multidimensional utility instrument (score range: –0.04 [worse than death] to 0 [death] to 1.0 [full health]). Linear mixed models estimated annual changes in QoL. Differences in trajectories were modelled with interactions for age and sex with adjustment for initial stroke severity. Model coefficients presented are annualised change in QoL units.

Results: Follow-up was complete for 90 percent (277/307) at 2 years, 84 percent (425/505) at 5 years, 84 percent (326/390) at 7 years and 87 percent (256/293) at 10 years after stroke. QoL decreased for everyone overtime but the rates of decline differed by age and sex. In those aged under 75 years at onset, the decreases per year were somewhat greater for women (Beta –0.015, 95 percent CI –0.010, –0.021) than men (Beta –0.012, 95 percent CI –0.007, –0.017). In those aged over 75 years at onset, the decreases per year were larger but the same in men (Beta –0.027, 95 percent CI –0.036, –0.018) and women (Beta –0.028, 95 percent CI –0.035, –0.021).

Conclusions: QoL deteriorates for all survivors of stroke over time, particularly older people at stroke onset. Determining what modifies this deterioration could improve the lives of those living with stroke.

1239

Higher Latitude Significantly Predicts an Earlier Age of Disease Onset in Multiple Sclerosis

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Background: Age at onset (AAO) in multiple sclerosis (MS) may be an important marker of disease severity and may have prognostic significance. Understanding what factors can influence the AAO may shed light on the aetiology of this complex disease and how age impacts the clinical presentation.

Objective: The aim of this work was to evaluate the association of latitudinal gradient and the AAO in MS population.

Methods: The study cohort of 20,636 eligible cases from 11 countries was extracted from the MSBase Registry. Only clinically definite MS (CDMS) patients aged >16 years were included. To

reduce heterogeneity, only centres with greater than 200 registered CDMS cases and of largely European descent were included. AAO was defined as the year of the first symptom suggestive of inflammatory central nervous system demyelination. Predictors of AAO were evaluated by linear regression.

Results: Compared with those living in lower latitudes, onset of symptoms was earlier than those at higher latitudes ($p = 2.51 \times 10^{-10}$). A reciprocal relationship was seen for ambient UV, with a significant decreasing age of onset for MS patients with each lower quartile of ambient UV ($p = 9 \times 10^{-8}$). For other demographic factors like sex, we found that AAO of female patients were approximately half year earlier than male patients ($p = 0.003$). AAO of progressive-onset MS patients were about 9 years later than bout-onset ones (2.4×10^{-273}).

Conclusion: An earlier AAO in higher latitudinal regions was found in this worldwide European cohort and correlated with variation in latitudinal UVR. These results suggest that environmental factors which act at the population level may significantly influence disease severity characteristics in genetically susceptible populations.

1248

Evidence of Stable Incidence of Aneurysmal Subarachnoid Haemorrhage in Tasmania, Australia Over the Last 20 Years

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Objective: There have been few studies of the changes in incidence of aneurysmal subarachnoid haemorrhage (aSAH). The most recent study, conducted in the UK, reported that incidence had not changed between 1981–84 and 2001–04. Recent changes in population distribution of risk factors for aSAH warrant updated incidence studies.

Methods: A retrospective study capturing all cases of aSAH across the island state of Tasmania, Australia (population 515,000) that has a single neurosurgical unit. Between 2010–14, potential cases of aSAH were identified using keyword medical record searches of admission and discharge lists. The 1996 Australian census population aged >15 years was used for calculation of age standardized rates (ASR per 100,000) and 95% confidence intervals to allow comparison with a previously published estimates of incidence from 1995–98.

Results: There were 1012 potential cases of aSAH identified from the multiple sources with 175 incident cases identified (66.9% female, Age 58.32 ± 16.14 years). The crude overall rate was 8.40 per 100,000 (5.65 in males, 11.09 in females). ASRs per 100,000 were 7.15 (95% CI: 4.02, 10.29) overall, 4.92 (95% CI: 3.28, 5.90) in males and 9.36 (95% CI: 7.59, 11.13) in females. These were marginally lower than ASR per 100,000 reported in 1995–98: overall 8.9; males 6.7; females 10.9.

Conclusions: Incidence of aSAH has remained relatively unchanged Tasmania over 20 years, which is in contrast to other

forms of stroke. This may be explained by concurrent decreases in some risk factors, such as smoking, but increases in other risk factors, such as diabetes. Efforts to reduce the incidence of aSAH should be promote, particularly given the poor outcomes associated with this disease.

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Incidence of Hospital-Admitted First-Ever Stroke Ho Chi Minh City, Viet Nam

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Background and Objective: Stroke is projected to be the second greatest cause of death in the world by 2020. Planning for the future burden is a critical task for all countries. Developing countries are lacking data on the burden of stroke. Our aim was to estimate the incidence of hospital-admitted first-ever stroke in one developing country, Vietnam.

Method: Cases of stroke admitted to 115 People's Hospital, a major teaching hospital in Ho Chi Minh City (HCMC) from December 2009 to December 2010 were registered with information recorded on type, previous history and severity of stroke. GIS software geocoded residential addresses and population data from the national Census was used to estimate hospital-admitted incidence of stroke. Incidence rates were age-standardised to the new World Standard Population.

Result: Among 5,017 registered cases of stroke, 3,083 were recorded among HCMC residents (53.4 percent males, 75.9 percent ischaemic stroke, 74.3 percent first-ever) with mean age 61.6 (SD 13.2) years for males and 68.5 (SD 13.3) years for females. The majority (77.5 percent) had moderate-to-severe disability on admission. In a high density catchment area surrounding the hospital, the age-standardized stroke hospital-admitted incidence was 124.1 (95 percent confidence interval CI 99.7, 148.5) per 100,000 for males and 101.6 (95 percent CI 74.8, 128.4) per 100,000 for females.

Conclusion: Estimated incidence of hospital-admitted first-ever stroke was low, probably due to under-ascertainment of mild and severe cases in this hospital-based study. The relatively young age of hospital-admitted stroke patients and high proportions with more severe stroke suggest that stroke imposes a high burden on the healthcare system and society in Viet Nam.

Mortality, Disability and Health-Related Quality of Life at 3 Months after First-Ever Stroke in Ho Chi Minh City, Vietnam

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Objective: The outcomes for people that suffer stroke in Vietnam have not been examined. We assessed mortality, functional status and health-related quality of life (HRQoL) of a cohort of stroke patients in Ho Chi Minh City, Vietnam.

Method: First-ever stroke patients from a stroke unit between June to September 2012 were assessed for socio-demographics, co-morbidity, lifestyle risk factors and stroke severity (National Institutes of Health Stroke Scale, NIHSS). Outcomes were measured by face-to-face interview in the patient's home 3 months following discharge including functional status with the modified Rankin Scale (mRS) and HRQoL with the EQ-5D.

Result: We recruited 450 consecutive patients (47.9 percent were female, mean age 62.5 [SD 14.0] years, 76.2 percent had ischaemic stroke). Three-month case-fatality was 10.4 percent. At 3-month follow-up of 376 patients, the mean mRS score at 3 months was 2.4 (SD 1.4) with 43 percent classified as 'dependent' (mRS greater than 3). Among 372 stroke survivors who were assessed HRQoL at 3 months, the mean EQ5D utility score was 0.67 (SD 0.33) and the mean EQ5D visual analogue scale score was 61.3 (SD 20.4).

Conclusion: Survival at 3 months post-discharge was relatively high but dependency was also high and HRQoL was lower than that of the general population in Vietnam. With the numbers of strokes occurring in developing countries like Vietnam predicted to increase in coming years, these outcome data suggest that the potential burden on society is likely to be high. It will be important to ensure that the healthcare system, and society more broadly, is equipped to manage the ongoing needs of those with stroke and their families.

Stroke Distribution Patterns and Characteristics in Kenya's Leading Referral Hospitals: Kenyatta National Hospital and Moi Teaching and Referral Hospital

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Objectives: Cardiovascular diseases (CVDs) are the second leading causes of morbidity and mortality in Kenya. However, there is limited information on cerebrovascular disease to support effective decision making and intervention efforts. This study sought to determine the magnitude and nature of stroke, and the associated risk factors in Kenya's two leading referral hospitals, as a basis for piloting a national stroke registry.

Methods: This was a prospective cohort study conducted in Kenyatta National Hospital (KNH) and Moi Teaching and Referral Hospital (MTRH) among confirmed cases of stroke within a six months period. The study utilized a modified World Health Organization STEPwise approach to stroke surveillance tool in collection of data on incidence, major risk factors, morbidity and mortality trends, and intervention strategies.

Results: A total of 348 patients were recruited [KNH 225 (m: 39.6%; f: 60.4%); MTRH 123 (m: 48.8%; f: 51.2%)]. Both hospitals recorded higher ischaemic (KNH 51.8%; MTRH 70.7%) than hemorrhagic stroke in both sexes. At day 10, KNH recorded 17.4% mortality while MTRH had 14.3%. The leading risk factors were hypertension (m: 73.0%; f: 74.7%), diabetes (m: 12.8%; f: 15.2%), and smoking (m: 28.9%; f: 11.1%). Majority of patients were on statins (ischaemic 65%, hemorrhagic 26.2%), and discharged on anti-hypertensives (ischaemic 48.4%; hemorrhagic 69.1%).

Conclusions: The observed high cases of stroke and risk factors highlight the need to strengthen the health system especially at the primary care level to accommodate screening and management of hypertension and other associated CVD risk factors, in addition to awareness creation at the community level. Further studies are necessary to determine the true burden of stroke at community level and explore health seeking behaviors in respect to CVDs in Kenya.

Multiple Sclerosis Prevalence and Preserved Sausages: A Global Ecological Study

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Objectives: In 15 countries which cover the whole globe, a geographical association has been shown between smoking (and curing) of meat and sausages, and the prevalence of multiple sclerosis (MS). In 2010, a textbook of home production of meat and sausages has been published (by S. and A. Marianski) which gives abundant and detailed informations on this particular subject. These data were used to subdivide the process of curing and smoking in order to find the most relevant factors, in particular the role of smoking at different temperatures.

Methods: In the textbook, 162 detailed recipes are given in a standardized way, and in 142 nitrite was used for curing. In 62 recipes, other details precluded the present evaluation (e.g. fresh sausage; hams; fish sausage; sausages of other meat than red meat or poultry; head cheeses) thus leaving 80 recipes for evaluation. They were subdivided by region of origin into: (a) developed countries of Northern and Central Europe and North America, having a high MS prevalence ($n = 63$); and (b) Southern European countries with medium MS prevalence and developing countries, having a low MS prevalence ($n = 17$). A four – fold table χ^2 – analysis was performed, and the final p – value was considered significant if $p = 0.05$, or lower.

Results: Both warm-/hot – smoked (at higher than 39°C) ($\chi^2 = 30.42$; $p < 0.0001$) and cold – smoked (at lower than 23°C) ($\chi^2 = 24.17$; $p < 0.0001$) varieties were significantly overrepresented in developed vs. Mediterranean/developing countries, respectively.

Conclusions: On the global scale, the preservation of sausages with warm- or hot – smoke vs. air – drying and/or marinating was correlated, with high significance, to the MS prevalence. Confounding, however (e.g. by climate; socio – economic status) must be born in mind.

10-Year Trends in Incidence of First-Ever Stroke and Stroke Sub-Types from the Auckland Regional Community Stroke Study 2002–2011

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Objective: To describe 10 year trends in the incidence of major stroke types and ischaemic stroke subtypes from the Auckland Regional Community Stroke Studies; ARCOS III (2002–2003) and ARCOS IV (2011–2012).

Methods: The ARCOS III and IV studies are a population-based register of all new stroke cases in the Auckland region over two 12-month periods. Strokes were subdivided into pathological subtypes (ischaemic stroke [IS], primary intracerebral haemorrhage [PICH], subarachnoid haemorrhage [SAH]). IS aetiological subtypes were classified using TOAST criteria into: large-artery atherosclerosis (LAA); cardioembolism (CE); small-vessel occlusion (SVO); stroke of other determined aetiology (OA); and stroke of undetermined aetiology (UND). Rate ratios (RR) were calculated with 95% confidence intervals (CI) per 100,000 people.

Results: In 2011 there were a total of 1634 first-ever in a life time strokes (52% females). Of these 81% were IS, 13% PICH, 5% SAH and 1% UND. Of IS subtypes, 29.1% were CE, 21.1% SVO, 14.7% LAA, and 35% OA and UND. CE was the most prevalent IS subtype of known aetiology in females (35%) while SVO was predominant in males (22%). Between 2002 and 2011, there were significant decreases in the age standardised incidence rates of first ever stroke (RR 0.86, 95% CI 0.80, 0.93), SAH (RR 0.73, 95% CI 0.54, 0.99) and UND (RR 0.14, 95% CI 0.09, 0.22). There was also an increase in the incidence of LAA (RR 2.32, 95% CI 1.73, 3.10) and SVO (RR 1.76, 95% CI 1.42, 2.19).

Conclusions: There was a significant decline in first-ever stroke incidence rates over a decade in Auckland. However, the increases seen in LAA and SVO indicate a need to enhance primary vascular prevention.

Topic 04. Treatment / Management

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Does Patient Age Influence the Quality of Care Received by Patients with Acute Stroke?

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Objectives: To assess whether the quality of care received by patients with stroke admitted to acute care hospitals varied by age group.

Methods: Quality of care was assessed for patients admitted to 40 hospitals registered in the Australian Stroke Clinical Registry (AuSCR; 2010–2013). Primary outcomes were the processes of care (POCs) recorded in AuSCR: admitted to a Stroke Unit (SU); received tPA if an ischemic stroke; prescribed antihypertensive medication at discharge; or received a discharge care plan if discharged to the community. Age was categorised into 5 groups and each group compared to the rest of the sample. Multivariable analysis was used to assess the association with outcome. Models were adjusted for gender, previous stroke, in-hospital stroke, socioeconomic status, stroke type, stroke severity and patient clustering.

Results: Data were available for 14571 episodes of care (47% female, 64% ischaemic stroke). Age was associated with receiving each of the POCs with variations in the direction of the association age by subgroup. Those aged 65–74 years were most likely to receive recommended POCs, especially SU care (aOR: 1.27, 95% CI: 1.13, 1.43) and tPA (aOR: 1.29, 95% CI: 1.10, 1.51). Age >84 years was associated with a reduced odds of receiving SU care (aOR: 0.74, 95% CI: 0.66, 0.82), tPA (aOR: 0.59, 95% CI: 0.50, 0.70) and a discharge care plan (aOR: 0.75, 95% CI: 0.65, 0.87). Aged <55 (aOR: 0.36, 0.32, 0.41) or age 55–64 years (aOR: 0.81, 85%CI: 0.72, 0.92) were associated with not being prescribed antihypertensive medication.

Conclusion: Our results confirm that age bias may exist with regards to stroke care delivery in Australia. This bias is not always specific to older patients.

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The Swedish National Neurology Registers

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The Swedish National Neurology Registers have developed from the Swedish National Multiple Sclerosis Register (SMSreg) that started almost 20 years ago to develop an equal health care of high standard. The selection of registered data in SMSreg had a connection to quality demands, expressed by the Swedish Social Board. Eventually SMSreg developed into a large web-based register (Compos platform), that easily could be changed when new definitions, treatments or effect variables entered the arena. SMSreg also contained excellent properties for MS research with its 14,000 included patients, and it was made accessible for researchers to collect data after approval of the Register Research Board. The possibility to evaluate side effects and long term outcome of specific immunomodulating drugs was valuable, and generated a separate project in the register, IMSE. In the web it was also possible to create a direct connection to the Medical Product Agency for immediate reporting of side effects. The use of certain drugs with high risks was connected to a demand to register in SMSreg in order to facilitate a national surveillance. SMSreg was also useful for pharmacoeconomic purposes. Recently, PROMs, i.e. patient reported outcomes, were introduced, with carefully chosen instruments that can be used from IT-systems in the clinic, or from the patients' homes. The aim is to facilitate follow up, to increase data density and increase compliance. Recently, a visualized analytical platform was launched, where individual effect variables are presented, compared with mean values of the MS population. MSSS, a computerized comparison of the individual disability score (EDSS) to mean EDSS, has also been entered to simplify the evaluation of the patient's progress. In 2014, several neurological diagnoses were entered into Compos, constituting the Swedish National Neurology Registers for MS, narcolepsy, motorneuron diseases, inflammatory polyneuropathies, vascular headache, epilepsy and myasthenia gravis.

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Associations between Serum Lipids and Apolipoproteins and Disability in Multiple Sclerosis

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Background: There is accumulating data suggesting an association between serum lipids & apoproteins and disability in MS.

Objective: To investigate the associations between serum lipids, apoproteins and disability in MS (actual disability and progression in disability).

Methods: A cohort (n = 178) with clinically definite MS were prospectively followed from 2002–2005 with biannual reviews (25(OH)D, and serum lipid and apoprotein levels). Disability was assessed annually by Expanded Disability Status Scale (EDSS) and MS Severity Score (MSSS). Associations with disability and progression in disability were evaluated using linear regression and multilevel mixed-effects linear regression, respectively.

Results: In basic analyses, nearly all lipid-related variables were associated with baseline clinical disability measured as EDSS and MSSS. In a fully adjusted model (age, sex, relapse at the time of review, BMI, smoking, physical activity and statin use), total cholesterol (p = 0.035) and ApoB (P = 0.003) were associated with EDSS and total cholesterol (p = 0.003), LDL (p = 0.001), nonHDL (p = 0.003), LDL/HDL ratio (p = 0.019), ApoB (p = 0.003) and ApoB/ApoA-I ratio (p = 0.018) were independently associated with MSSS. A higher disability might result in a more adverse lipid profile rather than vice versa, because adjustment for BMI and physical activity substantially reduced the associations. Higher BMI was significantly associated with higher EDSS (p = 0.006) and MSSS (p < 0.001). In analyses of change in disability, total cholesterol/HDL ratio (p = 0.029) was prospectively associated with subsequent annual change in EDSS.

Conclusion: In this prospective population-based cohort study, adverse lipid profile was associated with greater MS disability and disease progression. Improving the serum lipid profile may be beneficial for MS patients, both to improve their neurological condition and reduce the risk of vascular comorbidities.

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Prevalence and Factors Associated with Anxiety, Depression and Fatigue Five Years after a First Clinical Diagnosis of Demyelination

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Background: Anxiety and depression are common in multiple sclerosis (MS). We evaluated the prevalence and factors associated with anxiety, depression and fatigue, five years after a first clinical diagnosis of demyelination.

Methods: Cases with a first clinical diagnosis of demyelination were recruited and followed annually thereafter. A variety of other environmental/behavioural and clinical covariates were measured at annual reviews. Anxiety and depression were measured at five-year review by Hospital Anxiety & Depression Scale (HADS) and fatigue by Fatigue Severity Scale (FSS).

Results: Of the 236 cases, 40.2% had clinical anxiety (median HADS-A: 6.0), 16.0% had clinical depression (median HADS-D: 3.0), and 41.3% had clinical fatigue (median FSS: 4.56). The co-occurrence of all three symptoms was 3.76 times greater than expected by chance (observed 9.8%, expected 2.6%, p < 0.001). Younger age, higher disability, concussion or other disease diag-

nosis were independently associated with a higher anxiety score; male sex, higher disability, being unemployed, less physical activity, and antidepressant and/or anxiolytic-sedative medication use were independently associated with a higher depression score; and female sex, higher disability, immunomodulatory medication use, other disease diagnosis, and anti-depression medication use were independently associated with a higher fatigue score.

Conclusion: These results support previous findings of the commonality of anxiety, depression and fatigue in cases soon after first clinical diagnosis of demyelination and the clustering of the three symptoms, suggesting that they are part of the disease process. Early identification is critical.

1260

Eye Blinks to iPad: The Identification of Supports for Best Outcomes Using Interaction Analysis (IA)

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Background: An acquired brain injury (ABI) can result in a person having complex communication needs (CCN). Speech, which uses fine and sequenced motor movements, is only one vehicle for thought. There are also non-speech methods, referred to as augmentative and alternative communication (AAC). Communication displays and devices form a body of AAC known as aided communication. Research indicates that successful use of a communication device relies on both the capacity of the person with CCN and the able bodied person in the interaction (the communication assistant).

Objectives: This interactive paper examines components of interaction which impact on the prescription and support of communication devices for people with CCN arising from ABI. Recommendations are made for consideration by health care practitioners, service providers and agencies that fund trial and procurement of communication equipment.

Method: A review of the literature identifies key features of aided communication over the last fifty years. Interaction analysis (IA) is applied to four domains of interaction to identify areas of support which can be applied at the stages of prescription and intervention to improve outcomes. Audio-visual illustrations highlight the application of IA in this process.

Results: Communication, technology and human interaction are all dynamic complex systems. Components of these complex systems are identified, illustrated and discussed with view to improving outcomes for people with ABI and their communication assistants.

Conclusion: Despite technological advancements the AAC literature reports that communication devices may still be abandoned for a variety of reasons. Further, that a 'hope and pray' approach to prescription and provision is not conducive to best practice. This paper presents information which has implication for communication device developers, prescribers, interventionists and funders of communication equipment.

Effectiveness of an Intervention for Managing Patients' Needs Following Stroke: A Randomised Controlled Trial

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Objectives: To determine the effectiveness of an organised model of care for ameliorating the long term needs of patients with stroke or transient ischaemic attack.

Methods: Shared Team Approach between Nurses and Doctors For Improved Risk Factor Management (STANDFIRM) trial is an on-going prospective, multicentre, cluster-randomised controlled trial of risk factor management in people with stroke. Patients aged 18 years or older were included if they were hospitalised for stroke or transient ischaemic attack. We excluded patients recruited to another trial, or admitted from or discharged to a nursing home. The intervention comprised a comprehensive, team-based, individualised secondary prevention management program, including nurse-led education and support component, and regular specialist and general practitioner review of care plans. Patients were enrolled in this sub-study after completing their participation in the STANDFIRM trial (2 years). The primary outcome is a report of at least one 'unmet' need after a two-year follow-up period. Needs are measured across health, social and financial domains, via a mailed survey. A sample size of 320 was required to detect a difference of 10% in the proportion of patients reporting unmet needs between groups. Logistic regression will be undertaken to estimate the effect of the intervention on the reported unmet needs together with 95% confidence interval.

Results: The current response rate for the mail survey is over 70%. Data lock will occur in October 2015.

Conclusions: With a high response rate, the study has sufficient power for its primary outcome measure. Findings from this study could provide evidence on how to support survivors of stroke following discharge into the community from hospital.

Topic 05. Neurosurgery

Systematic Review of Economic Studies on Deep Brain Stimulation for Parkinson's Disease

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Background: Parkinson's disease (PD) is a debilitating neurological condition, which can be effectively managed with Deep Brain Stimulation (DBS). High-quality economic evaluations (EEs) are necessary to test the cost-effectiveness of DBS. However, the quality of the economic literature is mixed. A systematic review of EEs, which compared DBS with alternative treatments, was conducted.

Methods: Medical Subject Headings and terms relevant to PD, DBS, pharmacotherapies, and EE were used to search the Cochrane, PubMed, CINAHL and EconLit databases. Initially, 4,699 papers were identified. Studies that did not use a comparative design to evaluate DBS were excluded. Ten evaluations met our inclusion criteria. Two authors (TTHD&DR) independently assessed their quality. Trial-based models were evaluated using Drummond's Checklist and decision-analytical models were evaluated using Phillips' Checklist. All costs were converted into international dollars (\$) using the Purchasing Power Parities. Costs, quality-adjusted life years (QALYs) and Incremental Cost-Effectiveness Ratios (ICERs) were adjusted to the 2014 values.

Results: Quality of the EEs assessed was variable, especially the decision models. DBS costs estimated from trial-based studies are lower than those from decision models (\$31,658-\$192,446 vs. \$25,446-\$706,908). The costs of ablation and pharmaceuticals, were significantly lower than DBS. The QALYs gained from DBS ranged between 0.033-1.39 in trial-based models and 2.75-12.2 in decision models. The ICERs for DBS were between \$9,620-\$768,792/QALY. Five studies reported ICERs above the accepted ICER threshold in the UK (\$30,160-\$45,240/QALY) while four studies reported ICERs below this threshold. One did not report the ICER as cost per QALY.

Conclusion: The review suggests considerable variance in the cost per QALY. Further investigation into the appropriate models, cost estimates, and populations is required.

Topic 06. Neurorehabilitation

1269

Increased Cortical Plasticity in Rats' Periinfarct Tissue at 14 Days after Stroke

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Background and Aim: In industrial countries, stroke is the leading cause of disability and one major consequence is motor impairment. Successful re-learning of lost motor functions relies on cortical plasticity. Broad evidence points to increased cortical plasticity in the periinfarct tissue early after stroke that declines over time. Yet the precise time course is not known, but a better knowledge of this time course may be crucial to further improve neurorehabilitation therapies.

Method: We investigated the potential for synaptic plasticity in the periinfarct tissue following photothrombotic lesions in the primary motor cortex of rats. Synaptic plasticity – measured as long-term potentiation (LTP) – was induced by theta burst stimulation in the affected and intact hemisphere simultaneously at 1 – 3, 7, 14 and 28 days after photothrombotic stroke.

Results: LTP was increased in the periinfarct tissue 14 days after stroke ($p = 0.0013$) but remained unchanged at any other time point.

Conclusion: Our results point to a narrow time window of increased cortical plasticity in the periinfarct tissue around 14 days after stroke. These results may direct future research to further narrow down this potentially short critical time window for neurorehabilitation.

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Behavioural Intervention in People with Multiple Sclerosis: One Year Follow-Up

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Background: The aetiology of multiple sclerosis (MS) is not fully understood but includes environmental and genetic components. Evidence suggests a pivotal role for modifiable behavioural factors in disease progression and quality of life (QoL), however very little research is undertaken to assess the potential benefits of behavioural interventions (BIs) over time.

Objectives: The aim is to compare self-reported health outcomes (disability, relapse rate and QoL) in people with MS (PwMS) at baseline and 1 year post BI, and assess whether these

outcomes are related to self-reported adherence to the intervention.

Design Methods: 95 PwMS were enrolled in a BI (5-day residential retreat) designed to promote smoking cessation, regular exercise, healthy diet, adequate vitamin-D supplementation, and stress-management. For this ongoing longitudinal study, 87 participants completed online questionnaires including the MSIS-20 and MSQOL-54 to evaluate their adherence and health outcomes 1 year post BI. Data points were compared using paired t-tests.

Results: Compared to baseline, 1 year post BI participants reported a decrease in average physical disability (MSIS-20 scores from 33.8 to 31.7 ($p = 0.03$, $N = 71$)), a decrease in annual relapse rate from 1.0 to 0.2 ($P < 0.001$, $N = 56$ [relapsing remitting subgroup]), and increases in physical health- (7.9 points, $p < 0.001$, $N = 74$), and mental health- (8.5 points, $p < 0.001$, $N = 72$) related QoL. Self-rated adherence was higher among those with decreased vs. increased disability (7.7 vs. 6.4, $p = 0.005$).

Conclusions: For chronic diseases like cardiovascular disease and type-2 diabetes, BIs are already well developed and recognised, but in MS more confirmatory longitudinal data are needed. Our results, showing improved health outcomes 1 year after BI, provide preliminary evidence for a sustainable secondary preventive strategy for the ~2.5 million PwMS worldwide.

Topic 07. Healthcare

929

Impact of Language Barriers on Stroke Care and Outcomes: Evidence from the Australian Stroke Clinical Registry (AuSCR)

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Objectives: Stroke has devastating consequences at all ages and among patients with language barriers this may impact more substantially on health-related quality-of-life (HRQoL). We aimed to compare patient characteristics, quality of hospital care indicators, and outcomes between patients who did and did not require an interpreter.

Methods: Data from the Australian Stroke Clinical Registry (AuSCR) obtained January 2010 to December 2013 ($n = 40$ hospi-

tals). Multilevel regression models were used in group comparisons. HRQoL was assessed with the EQ-5D-3L and EQ5D visual analogue scale (VAS) at 90–180 days.

Results: Among 16,887 registrants, 701 (4.1%) required an interpreter. Compared to patients without language barriers, patients with language barriers were more likely to be aged 75 years or older (69% vs. 52%, $p < 0.001$) and be unable to walk on admission (72% vs. 61%, $p < 0.001$). Patients with language barriers had greater access to most quality indicators (stroke unit care 84% vs. 76%, $p < 0.001$).

After accounting for patient characteristics and stroke severity, patients with language barriers had comparable discharge outcomes (e.g. mortality, discharged rehabilitation) to patients without language barriers. At median 101 days post stroke, patients with language barriers reported more problems with mobility (65% vs. 50%), self-care (56% vs. 32%), activity (73% vs. 57%), pain (66% vs. 49%) and anxiety or depression (60% vs. 46%) and lower median VAS score barriers (median 60 vs. 71; $p < 0.001$ for all comparisons).

Conclusions: Patients who had language barriers presented to hospital with more severe strokes and although they received good access to quality stroke care they experienced poorer HRQoL after stroke. Determination of the underlying reasons for such differences in severity and outcome may be of value in the care of patients with stroke who require an interpreter.

1023

Evolution of a Stroke Data Monitoring System to Improve Stroke Care Quality in Australia: The New Frontier

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Objectives: Data collection is important to monitor and support quality improvement. Data collection in hospitals, for monitoring stroke care and patient outcomes, is complicated by clinicians often using multiple systems to collect the same variables on the same patients. Creating a single, yet flexible, data collection system was proposed to avoid inefficiencies, improve data quality and encourage greater participation in national data collection programs.

Methods: In 2013, the Australian Stroke Coalition agreed to focus efforts on improving the sustainability of data collection for quality monitoring in Australia and established the Data and Quality Working Group. The data custodians from major stroke care quality programs ($n = 3$) and research projects ($n = 5$) were invited to work with the National Stroke Foundation (NSF) to design a unified web-based system for monitoring stroke care.

Sub-committees were established to focus on-governance+ a comprehensive national data dictionary to ensure standardization of variables+ webtool features and functionality+ policies and procedures+ communication+ and, funding strategies. Staged transition of the programs is planned since governance clearances differ.

Results: Agreement to support data collection within a single webtool infrastructure was achieved across all existing national program data custodians- NSF Audit+ Australian Stroke Clinical Registry, reperfusion data collection programs e.g. SITS+ imaging database (INSPIRE)+ and some state-based programs e.g. Victorian Stroke Telemedicine Program, New South Wales Stroke Clinical Audit Program. The Australian Stroke Data Tool was inaugurated for the NSF national audit in June 2015. Implementation and transition plans for the Australian Stroke Clinical Registry and other programs are underway.

Conclusion: Through shared vision, good will and collaboration, a unified web-based system for national stroke data collection for multiple partner programs has been developed, and will improve data collection efficiency. The potential uses and value of this tool will be substantial.

1154

Awareness and Healthcare Seeking for Stroke in Rural Gadchiroli, India: A Community-Based Study

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Objectives: With epidemiological transition stroke is emerging as a public health priority in rural India. However, information on healthcare seeking for stroke from population-based studies from rural India is rare. In this study we evaluated the awareness and healthcare seeking for stroke in rural Gadchiroli, India.

Methods: In a cross-sectional survey, trained surveyors screened a well defined population of 45,053 individuals living in 39 villages in Gadchiroli district for symptoms of stroke. A trained physician and a neurologist evaluated screen positive patients and diagnosed stroke. Information on healthcare seeking was obtained from patients with stroke using a structured questionnaire.

Results: In the screened population, 175 patients had stroke. Awareness about stroke was low with only 10.3% patients knowing the aetiology or the risk factors for stroke. A majority (97.7%) of the patients had sought some treatment after acute stroke. In about half (53.71%) of the patients informal providers or herbal medicine providers were the first healthcare providers after acute stroke. The herbal medicine providers were the most frequent providers with 76.57% of the stroke patients seeking care at least once from them. One third of the patients (34.86%) visited the government-run district hospital where a brain imaging facility is available and only 12% patients had brain imaging done after the stroke. Very few patients (3.43%) were on anti-platelet agents at the time of evaluation.

Conclusion: Our study indicates a significant gap in care for stroke in rural Gadchiroli. The awareness for stroke needs to be increased and the facilities to provide acute as well as long term care after stroke need to be developed and made accessible in rural India to reduce the burden of stroke.

Topic 01. Prevention

1277

Occurrence of Idiopathic Hypersomnia and Narcolepsy Type II after Pandemrix Vaccination in Sweden and Finland

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Objectives: Epidemiological studies from Sweden and Finland, and also from other countries, have shown an increased incidence of narcolepsy after the vaccination against the swine flu, H1N1 autumn 2009. The incidence of other sleep disorders such as idiopathic hypersomnia and narcolepsy type II has to our knowledge not yet been investigated in relation to the Pandemrix vaccination. There is no certain knowledge of the pathophysiology of these disorders. We wish to raise the question if immunologic events can trigger these disorders and plan future systematic studies on these issues.

Method: The Finnish Narcolepsy database (NARPA) was systematically searched for cases debuting with hypersomnia after Pandemrix vaccination defined by MSLT-sleep latency under 8 minutes. Additional cases were gathered by one of the authors from two sites in Sweden. The investigations were reviewed to exclude other causes of hypersomnia.

Results: 9 cases were included, all with debut within three months after vaccination. 6 subjects showed evidence of Idiopathic hypersomnia and 3 had narcolepsy type II. 4 were found HLA-DQB1:0602 positive without any association to diagnosis. DSPS was found in 2 males and 2 females. 1 case suffered streptococcal infection after the Pandemrix vaccination and tested positive in a PANDAS-assay.

Conclusion: The study suggests that hypersomnia and/or Narcolepsy type II can be caused by immunologic triggers such as Pandemrix vaccination alone or in combination with infections. No systematic screening for infections was conducted which we plan to do in future studies. We do advocate caution in interpreting the findings due to the difficulty in classifying the heterogeneous condition known as idiopathic hypersomnia and also the finding of these cases could be associated with the bias of increased awareness of professionals and public in the suspected risk of narcolepsy or merely coincidental.

Topic 02. Diagnosis

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Optical Coherence Tomography (OCT) in Patients with Migraine

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Objectives: Assessment of Retinal Nerve Fiber Layer Thickness (RNFL) by Optical Coherence Tomography (OCT) in patients with migraine.

Methods: This prospective cross-sectional study of 34 consecutive patients, with migraine was recruited from the headache clinic of Madras institute of Neurology. RNFL thickness was measured using OCT. RNFL thickness was considered abnormal if Average RNFL thickness is <100 micrometers. They were analysed with duration of migraine, number of episodes per month and duration of each episode (duration <5 and ≥5, number of episodes <10 and ≥10, duration of each episode <12 and ≥12).

Results: Among 34 patients, there was female preponderance [5 male and 29 female]. 7 patients (20.58%) had duration of headache <5 years, 27 patients (79.42%) had duration for ≥5 years, fifteen patients had <10 episodes month and twenty two patients had ≥10 episode, ten patients (29.42%) had <12 hours of headache and 24 patients (70.58%) had ≥12 per episode. RNFL thickness was reduced in 24 patients out of 34 (70.6%) in right eye in right temporal quadrant and it was reduced in 27 patients out of 34 patients (79.4%) in left eye in left temporal quadrant. RNFL thickness in temporal quadrant on both sides was significantly reduced if duration of migraine is ≥5 (p value 0.0062 & 0.0073), if number of episodes per month is ≥10 (p value 0.0097 & 0.013), and if duration of each episode is ≥12 hours (p value 0.015 & 0.0062).

Conclusion: RNFL thickness is reduced in the temporal quadrant of both eyes in migraine patients and is significantly correlated with duration of migraine, number of episodes per month and duration of each episode of migraine.

Electrophysiological Studies in Migraine

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Objectives: The diagnosis of migraine is a clinical task and there are no specific diagnostic tests. In our study, electrophysiological test battery such as VEP, ECG and P300 were done and correlated with duration, number of episodes per month and duration of each episode of migraine.

Methods: 31 patients of migraine were selected and subjected to VEP, ECG and P300. P100 latency and P100-N75 amplitude, ECG variables and P300 latency were recorded. They were analysed with duration of migraine, number of episodes per month and duration of each episode (duration < 5 and >5, number of episodes <10 and >10, duration of each episode <12 and >12).

Results: P100 latency and amplitude are significantly abnormal if duration is >5 years (p value 0.012, 0.04 for P 100 latency and 0.003, 0.03, P100-N75 amplitude), if no of episodes are >10 (p value 0.004, 0.006 and 0.007, 0.05) and if duration of each episode is >12 hours (p value 0.0002, 0.05 and 0.011, 0.05). p wave duration, ST changes and T wave inversion are significantly abnormal if duration of migraine is >5 years (p value 0.011, 0.05, 0.02), no of episodes >10 (p value 0.025, 0.011) and duration of each episode >12 hours (p value 0.031, 0.025, 0.008). P300 latency is significantly prolonged if duration >5 years (p value 0.043), no of episodes >10 (p value 0.03) and duration of each episode >12 hours (p value 0.007).

Conclusion: P100 latency, P100-N75 amplitude, ECG changes and P300 latency are significantly abnormal in patients with migraine and correlated with duration of migraine, number of episodes per month and duration of each episode of migraine.

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Usefulness of Duplex Sonography in Posterior Circulation Stroke

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Objectives: The aim of our study was to verify the usefulness of duplex sonography in posterior circulation (PC) stroke.

Methods: All the patients with acute PC stroke (onset ≤ 7 days), admitted for 4-year period and given complete evaluation including brain MRI, angiographic and duplex sonographic studies, were enrolled. According to sonographic findings of relevant extracranial vertebral artery, patients were classified into 3 groups as follows- (1) normal VA (NVO)+ (2) acute VA occlusion (AVO)+ (3) chronic VA occlusion or occlusion underlying hypoplasia (CVO). Baseline characteristics, symptoms and progression, etiology subtypes, lesion characteristics on imaging, and 3-month outcome were analyzed.

Results: Among 90 enrolled patients with PC stroke, 69 patients belonged to NVO, 9 to AVO, and 12 to CVO. Cerebellar

lesions were most frequent in CVO (hemisphere, 50%+ vermis, 33%), followed by AVO (hemisphere, 33%+ vermis, 11%+) and NVO (hemisphere, 17%+ vermis, 6%+ p <0.05). Modified Rankin Scale score of 3-6 at 3 months was most frequent in CVO (67%), followed by AVO (56%) and NVO (35%+ p = 0.03). Patients with bilateral VA lesions tended to have a progressive stroke (44%).

Conclusions: Duplex sonography of vertebral artery was useful and might help predict lesion location and clinical outcome.

Topic 03. Epidemiology

1106

Month-of-Birth Effect on the Risk of Multiple Sclerosis in Denmark

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Background: Several studies have shown seasonal variation of month of births in people with MS (PwMS) compared with the background populations.

Objectives: To assess the distribution of month of birth in all Danish PwMS patients compared with the monthly variation of birth in the Danish background population.

Methods: Information on month and year of birth of all Danish PwMS who were born 1930–1989 was retrieved from The Danish Multiple Sclerosis Registry. Statistics Denmark provided tables with year and month of birth for the entire Danish population in the same period.

Results: The number of PwMS, born 1930–1989 was 17,055. The number of non-MS individuals born within the same period was 4,284,537. PwMS followed the same pattern of month of birth as the entire Danish background population. Because leisure time sunlight exposure may have increased as a result of changes in life style during the six birth-decades in this study, we performed stratified analyses after dividing year of birth into three periods- 1930–1949+ 1950–1969+ and 1970–1989. Neither of these periods we found any statistical difference between PwMS and the background population (1930–1949- p = 0.21+ 1950–1969- p = 0.89+ 1970–1989- p = 0.49). No single month showed statistical significant deviation from the reference month.

Conclusion: Even when using birth data on all PwMS and on the population from an entire country over 60 years, we did not succeed in confirming the month-of-birth effect on the risk of MS, demonstrated in a number of studies from different geographical sites. Possible explanations may be that the physical seasonal changes in the coastal climate of Denmark are not strong, or the Danish population does not have the same susceptibility to seasonal physical changes in terms of risk of MS.

Molecular Characterization of Human Polyomavirus JC in Brazilian AIDS Patients with and without Progressive Multifocal Leukoencephalopathy

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Objective: To compare genotypes and adaptive mutations of JCV strains from Brazilian AIDS patients with and without PML.

Method: The VP1 region of JCV was amplified by polymerase chain reaction from cerebrospinal fluid samples from 51 patients with PML and from urine samples of 47 patients with AIDS without central nervous system disease. Genotyping was done by phylogenetic analysis. Amino acid replacement and selection pressures were also investigated.

Results: JCV genotype frequency distributions showed that genotypes 2 (32.7%), 1 (26.5%) and 3 (23.5%) were the most prevalent. Genotype 1 had a positive association ($p < 0.0001$) and genotype 3 showed an inverse association ($p < 0.001$) with PML. A previously undescribed point mutation at residue 91 (L I or L V) and (L P), non-genotype-associated, was found in 5.49 (10.2%) and 2.47 (4.3%) JCV sequences from PML and non-PML patients, respectively. This mutation was under positive selection only in PML patients. A previously described substitution of T-A in position 128 showed a significant difference between PML and non-PML cases (70% versus 16%, respectively, $p < 0.0005$).

Conclusion: In Brazilian patients with AIDS, JCV genotype 1 showed a strong association with PML ($p < 0.0001$) and JCV genotype 3 showed an inverse association with PML. The possible association of aminoacids substitution in residues 91 and 128 with PML in patients with AIDS must be further investigated.

1127

Can Exposure to Environmental and Lifestyle Risk Factors Bring Forward the Age of Dementia Onset?

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Objectives: The age at which dementia symptoms emerge has important implications, especially given that delaying onset by as little as two years could reduce worldwide prevalence by millions. Moreover, young onset dementia is associated with significantly greater burden than dementia in late life. Several environmental and lifestyle factors are known to increase risk of incident dementia, but whether preventing exposure to these could delay the onset of neuropathology and or emergence of symptoms is not known. The aim of this review was to determine whether poten-

tially preventable risk factors are associated with an earlier onset of dementia.

Methods: Academic databases were searched to March 2015 for studies assessing the impact of modifiable factors (e.g. education, cardiovascular illness, psychiatric illness, alcohol use) on the age of dementia symptom onset. Meta-analysis was performed for each risk factor where at least four studies used a comparable statistical technique.

Results: Thirty-seven eligible articles were identified. Stroke, smoking and more pregnancies were associated with a significantly earlier age of dementia onset, while bilingualism delayed onset. Despite being strongly associated with incident dementia, there was no consistent effect of education, hypertension, traumatic brain injury or diabetes on the age of dementia onset.

Conclusions: Stroke, smoking, fewer pregnancies and monolingualism are associated with a significantly earlier onset of dementia. Prevention programs focussed on these factors may forestall onset. Exposure to other factors known to be associated with incident dementia, such as low education or hypertension, may not be predictive of when neuropathology will begin to accumulate or when symptoms will emerge.

1161

High Risk of Narcolepsy Amongst Children and Adolescents after Pandemrix Vaccination in the County of Östergötland, Sweden

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Objectives: Epidemiological studies from Sweden and Finland, and also the UK, have shown an increased incidence of narcolepsy after the vaccination against the swine flu, H1N1, in autumn 2009. A follow-up study until December 2011 with populations from seven regions area in Sweden demonstrated a three-fold increased risk of diagnosed narcolepsy amongst vaccinated in the age group ≤ 20 . Increased incidence of narcolepsy in children in the county of Östergötland, Sweden was previously observed by us, which gave reason to perform a case-control study of narcolepsy and Pandemrix vaccination in people aged ≤ 17 in this county.

Method: The study population included children born 1992 and later. Information of vaccinated children in this age group was derived from the Statistical Office of the County Council of Östergötland. The Pandemrix vaccine was given in October-December 2009 with a second dose in January 2010. Cases were incident from January 2010 to 31st December 2010. From all paediatric units in the county, children with the diagnosis of narcolepsy have been collected, and medical records have been studied.

Results: Altogether there were 20 children, 12 girls and 8 boys in Östergötland that had onset during the post vaccine period. There were 45 778 vaccinated and 41 355 non-vaccinated children. Of the 20 children diagnosed with narcolepsy, 19 had received the Pandemrix vaccine and only one child had not. The time distribution of diagnosis was from year 2010 to 2013. The Odds Ratio (OR) for vaccinated to non-vaccinated children was 17.7 (95% confidence interval: 2.7–147.5; $p = 0.0036$).

Conclusion: This study showed an association between Pandemrix vaccination and onset of narcolepsy in people aged ≤ 17 in one county of Sweden. Possible bias is the increased awareness by professionals during later years.

1236

Spontaneous Intracerebral Hemorrhage in Tibetan Plateau: How Different from Han Chinese in Chengdu Plain

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Background and Purpose: Spontaneous intracerebral hemorrhage (ICH) patterns in the Tibetans are little known. We investigated the characteristics of those patients, compared with Han Chinese patients in Chengdu Plain.

Methods: We enrolled consecutive patients with ICH who were admitted to West China Hospital (WCH) and People's Hospital of Garzê (PHG) within 1 month of stroke onset from January 2013 to December 2013, respectively. Basic characteristics and functional outcomes for ICH were compared between Tibetan and Han Chinese.

Results: Of the 843 cases included, 105 (12.5%) patients were from PHG and 738 (87.5%) patients were from WCH. Patients from PHG, compared with those from WCH, were older, more often had experienced hypertension, less often diabetes and current smoking, and had a longer admission delay (all $P \leq 0.010$). On admission to ICH, they also had higher systolic blood pressure and diastolic blood pressure, higher level of hemoglobin, platelets, and cholesterol, and lower level of serum albumin (all $P \leq 0.001$). Their imaging results showed more midline shift and less intraventricular hemorrhage (all $P \leq 0.05$). The overall death rates were similar between the two regions and Tibetans had a higher disability rate at follow-ups. After stratified by age, Tibetans had a more than 4-fold risk of death in the <55 group at follow-ups after multivariate analysis.

Conclusions: The ICH patients in Tibet differed in baseline characteristics from patients in a low altitude and had a higher disability rate on follow-up. The discrepancy of death rate emerged after age stratification.

1244

Characteristics of Guillain-Barré Syndrome Outcome at Cipto Mangunkusumo Hospital Jakarta

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Objective: The outcome of Guillain-Barré Syndrome (GBS) is not completely well, despite of the development of immunotherapy. Patients with poor outcome have to be identified quickly in order to determine next management in hospital and home care planning. Erasmus GBS Outcome Score (EGOS) is a model to predict the outcome of patients at six months after onset. Unfortunately, the EGOS studies were conducted in foreign countries, which have different patient characteristics and environment. This study was performed to document the outcome characteristics and EGOS of GBS patients.

Methods: We performed a cross-sectional study at Cipto Mangunkusumo Hospital, Jakarta, from January 2010 to December 2014. Using medical records, we reviewed demographic and clinical characteristics, EGOS, and outcome of GBS patients admitted to the hospital.

Results: We report new cases of GBS in this hospital were 7.6 cases/year. There was no seasonal variation of GBS onset. Male-to-female ratio was 1.2:1. Mean age was 39.71 years old. The most frequent variant was acute inflammatory demyelinating polyneuropathy (AIDP) (31.6%), followed by acute motor and sensory axonal neuropathy (AMSAN) (18.4%), acute motor axonal neuropathy (AMAN) (15.8%) and Miller-Fisher syndrome (MFS) (13.2%). Median duration of onset – hospital was 8.5 days. Twenty four patients were treated with plasma exchange, in which 83.3% got these two weeks after onset. Proportion of patients with good outcome was 64.3%. Patients with higher score of EGOS tend to have poor outcome.

Conclusions: This study shows that proportion of GBS patient outcome had a same data trend with EGOS. This proportion of patients with good outcome could be enhanced early diagnosis and prompt immunotherapy.

Physical Activity Compliance of Korean Adults with Chronic Diseases in Relation to Stroke

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Background: Proper physical activities are known to be helpful in the prevention and management of chronic diseases and stroke. However, the physical activity level of patients with chronic diseases is low. Therefore, this study aimed to investigate the physical activity compliance of patients with hypertension, diabetes, and dyslipidemia in relation to stroke.

Methods: This study analyzed the 2010–2012 Fifth KNHANES data. We included 13,873 individuals in the analysis. The level of physical activity compliance was measured by performing multivariate logistic regression analyses.

Results: In the univariate analysis, the subjects with hypertension, diabetes, or stroke tended to comply with the physical activity guidelines less faithfully than their healthy counterparts. The proportion of subjects with hypertension who were insufficiently physically active was 65.4% among the men and 75.8% among the women. For diabetes, the proportions were 66.7% and 76.8%. For stroke, the proportions were 85.2% and 82.3%, respectively. No significant difference was found between the subjects with dyslipidemia and their healthy counterparts. In the multivariate logistic regression analysis, no significant difference in physical activity compliance was observed between the subjects with hypertension, diabetes, dyslipidemia, or stroke and their healthy counterparts for both sexes.

Conclusions: The patients with hypertension, diabetes, or stroke tended to have lower physical activity prevalence than their healthy counterparts. However, for dyslipidemia, no significant difference was found between the two groups. Given the significance of physical activities in the management of chronic diseases related to stroke, the physical activities of these patients need to be improved.

The Most Frequent Cerebral Complaints and Arterial Hypertension in a Middle Aged Population

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Aim: To evaluate the prevalence and combinations of 'cerebral' complaints in the population of 40–59 years old people with and without arterial hypertension (AH).

Materials: 399 subjects (150 men, 270 women) were examined during cross-sectional population based study. 202 subjects were hypertensives, 197 normotensives. 32 combinations of five complaints (headache, vertigo, tinnitus, memory decline, mental working capacity decline) were calculated.

Results: Prevalence of each complaint was: headache 80.7% (equal in non-AH and AH subgroups), vertigo 40% (37% vs. 44%,

$p > 0.05$), tinnitus 32% (25% vs. 39%, $p < 0.05$), memory decline 47% (42% vs. 52.4%, $p = 0.049$), mental working capacity decline 48% (41% vs. 55%, $p < 0.05$). Number of complaints in one person was: 5 (7.6%), 4 (18.5%), 3 (23.5%), 2 (22.9%), 1 (21%), no complaints (6.5%).

The most prevalent combination in non-hypertensive and hypertensive group was the headache alone – 18.8 and 11.9% accordingly ($p > 0.05$). Second place – the combination of all complaints except tinnitus in non-hypertensives – 10.1% (10.9% in hypertensive group) and all 5 complaints together in hypertensives – 11.4% (4% in non-hypertensives, $p < 0.05$). No complaints was in 9.1% of non-hypertensives vs 5.4% ($p > 0.05$) – the third and forth places accordingly. Differences in prevalence of the other combinations were statistically nonsignificant.

Conclusion: The prevalence of complaints on tinnitus, memory or mental working capacity decline is higher in hypertensives. Headache alone remains the most frequent complaint. The second and the third places are for multiple complaints, but in arterial hypertension they include tinnitus more frequent. Objective neurological changes underlying differences in complaint's frequencies need to be studied.

Topic 04. Treatment / Management

Diabetes and Sleep Disorders: A Synergism That Complicates Neurological Treatment

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Objectives: Researchers are beginning to examine relationships shared by sleep disorders SDs and diabetes to illuminate relevant covariance. It is estimated that at least 9% of people worldwide have diabetes and many more have pre-diabetes. Daily self-management is essential for controlling diabetes and its associated complications. Further, research has demonstrated that SDs are associated with prolific health problems. The extent of these relationships has not been clearly ascertained because of significant rates of under or inadequate diagnoses along with a multitude of intervening variables associated with disease symptomatology. Investigations are further constrained by difficulty in acquiring valid data from people whose diagnoses are based on a nocturnal polysomnography (NP). Comorbidity of diabetes with SDs may present unique challenges for daily self-management because SDs may compromise cognition, emotional well-being, and general health.

Methods: We constructed a 111-item questionnaire to use in conjunction with nocturnal polysomnography (NP), the Epworth Sleepiness Scale (ESS), and medical chart reviews of people referred for evaluation of SDs.

Results: We analyzed data from 1002 participants (464 females, 538 males). Of these, 165 had a history of diabetes and were diag-

nosed with SDs. Analyses of the diabetes vs. no diabetes groups provided characterizations of similarities and differences. For example, the diabetes SD group was more likely to be diagnosed with poor sleep efficiency and nocturnal hypoxemia+ had higher BMI+ slept fewer hours+ spent more time in stage N1 and less in stages N3 and REM+ required higher CPAP pressure+ reported greater incidents of pain, depression, high blood pressure, heart failure, heart attack, chronic lung disease, thyroid disease, stroke, bed wetting, headaches, asthma, difficulty breathing, used more medications, and expressed more health concerns.

Conclusions: Recognizing diabetes risks and predictors associated with SD can facilitate prevention, early diagnosis, and effective treatment modalities.

1148

New Combination Therapy of Autologous Cord Blood Cell Therapy and Therapeutic Hypothermia for Newborn Hypoxic Ischemic Encephalopathy in Japan

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Objectives: Hypoxic ischemic encephalopathy (HIE) induced by perinatal asphyxia is an important neurological problem in the neonatal period and leads to neurological sequelae such as cerebral palsy, intellectual disorders and behavioral problems. We initiated new combination therapy of autologous cord blood cell therapy (ACBT) and therapeutic hypothermia (TH) for newborn HIE in Japan.

Methods: Infants admitted to the NICU of 6 hospitals in our research group will be eligible if they are ≥ 36 weeks gestational age and birth weight $\geq 1,800$ g with HIE and meet the cooling criteria. Umbilical cord blood (UCB) will be collected aseptically and prepared by using SEPAX. We will enroll infants in NICU who are cooled for HIE and for whom informed consent for ACBT has been confirmed. We will record UCB collection and cell infusion characteristics.

Results: UCB collection and infusion preparation in normal deliveries were as follows: (1) number of CD34 positive cells was more than 90%, and survival rate of CD34-positive cells remained at 99% at 72 hours after separation. (2) Rise of potassium after 72 hours due to events such as contamination of red blood cells was median 5.8 mEq/l (1.7–11.6). (3) In the separation at SEPAX, to set on the machine, the minimum requirement of cord blood volume was 40 ml, and exclusion criteria must be set for clotting of

cord blood collected at the time because valid cell separation and recovery becomes impossible.

Conclusions: Good results in UCB collection and infusion preparation were obtained when compared to the results of Cotten et al. [1] although there is a difference between high risk and normal deliveries. We started this clinical trial in December 2014.

Reference

- 1 Cotten CM, et al: J Pediatr 2014;164(5):973–979.

1213

Parkinson's Disease: Comparing Impacts on General Health and Well Being Experienced by Individuals with PD and Their Caregivers

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Objectives: The prevalence of Parkinson's disease (PD) is rising consistently with the increase in human life expectancy. Family members often assume the primary responsibility for individuals with PD (IwPD) and consequentially experience impacts on general health and well-being. Despite the challenge to quality of life (QoL) for both caregivers (CG) and IwPD, the impact on CGs is not well understood.

Methods: We constructed two questionnaires specified for IwPD (84 items) and their CG (81 items) utilizing traditional PD measures along with additional questions. Using a list of names provided by PD organizations, both were either mailed or emailed to 230 pairs. The questionnaires included a wide range of topics such as health history and change, physiological health, social engagement, support availability, stressors, emotional health, sleep, financial concerns, and overall QoL.

Results: We compared responses from IwPD (mean age 77.10) and CG (mean age 68.40). An example of findings: the CG group was more likely to be women, report higher incidences of depression, feeling lonely and isolated, anger, bitterness, anxiety, problems with close relationships, stress, and lack of support.

Conclusions: The presence of PD creates a multifaceted exponential increase in challenges to QoL for both IwPD and their CG. Moreover, in many instances the support for IwPD exceeds support for CGs who bear the physical and emotional burden of an illness they do not have. Maintaining a healthy QoL, while continuing to assist the IwPD is essential but difficult for CG to achieve. Identification of factors that create CG strain and Illustration of differences in perspectives of IwPD and their CGs potentially advances knowledge to address needs for the benefit of both parties. We hope avenues to accomplish this balance will be continued in future studies.

1229

Role of Clinical and Imaging Features in the Prediction of Clinical Outcome in Acute Cerebellar Stroke

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Introduction: Acute Cerebellar Stroke accounts for 2–3% of all strokes. Mortality is high in acute cerebellar stroke, due to complications such as brain stem compression and hydrocephalus.

Aim: To study about the role of clinical and imaging features in the prediction of clinical outcome in acute cerebellar stroke.

Methods: This study is a prospective analytical study carried out in stroke unit of Institute of Neurology, Madras Medical College, Chennai from January 2014 to April 2015.

The clinical and imaging features including the volume of acute cerebellar stroke at the time of admission, during the hospital course are monitored to analyse the clinical outcome.

Results: This study is done in 50 patients with acute cerebellar stroke – Ischemic stroke (58%), Hemorrhagic stroke (42%). Mean age in males (53.68), Females (62.00). Incidence in males (82%), Females (18%). Statistical analysis revealed Low GCS score was associated with poor clinical outcome ($p < 0.001$). Low NIHSS score was associated with good clinical outcome ($p < 0.001$). CT Brain is highly sensitive in detecting hemorrhagic stroke and its complications ($p < 0.001$). MRI Brain is highly sensitive in detecting ischemic stroke and its complications ($p < 0.001$). Management of brain stem complications in appropriate time showed good clinical outcome ($p < 0.001$). Cerebellar hemorrhage size < 3 cm showed good clinical outcome. 3–5 cm showed good clinical outcome with surgery. > 5 cm showed poor clinical outcome inspite of surgery ($p < 0.001$).

Conclusion: In acute cerebellar stroke, monitoring the clinical and imaging features help us to detect the complications early. Appropriate management in time gives good clinical outcome.

1241

Frequency of Comorbidities and Their Association with Clinical Disability and Relapse in Multiple Sclerosis

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Background: MS patients may be at an increased risk of comorbidities due to the debilitating and chronic nature of the disease. We aimed to investigate the frequency of comorbidities and their associations with clinical disability and relapse in MS.

Methods: A prospective cohort of 198 MS patients, followed 2002–2005, and queried about specific doctor-diagnosed comor-

bidities. Prevalences of comorbidities in the MS cohort were compared to the 2007 general population in Australia. Multilevel mixed-effects linear regression was used to assess the difference in subsequent disability between those who reported comorbidities and those who did not. The association with hazard of relapse was assessed using survival analysis.

Results: The age-standardised prevalences of hypertension, dyslipidaemia, asthma, psoriasis, eczema and anaemia were significantly higher in the MS cohort compared to the general Australian population. The level of disability (MSSS) in those who reported overweight obesity (β 0.76 (95% CI: 0.04, 1.48), $p = 0.037$), or dyslipidaemia (β 1.05 (95% CI: 0.07, 2.02), $p = 0.036$) was significantly higher compared to those who did not report these comorbidities, even after adjustment for potential confounders. There were no significant associations between comorbidities and change in disability. For relapse analyses, rheumatoid arthritis and anaemia were associated with more than three-fold (HR 3.70 (95% CI: 1.80, 7.58), $p < 0.001$) and two-fold (HR 2.04 (95% CI: 1.11, 3.74), $p = 0.022$) increased risk of subsequent relapse respectively.

Conclusions: The prevalences of some comorbidities were higher in MS patients and associated with greater disability and relapse risk. Treatment of these comorbidities in patients with MS has the potential to improve disease course and understanding of the prognosis and outcomes of MS.

1259

Interaction Analysis

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Research has identified that interactions between users of augmentative and alternative communication (AAC) and their communication partners/assistants has unique characteristics. Interaction analysis (IA) is a way of transcribing and analysing these differences to provide data which can be used for intervention mapping. This poster illustrates the four domains of interaction analysis and proposes ways of optimising best outcomes for users of AAC and the people they interact with.

Comparison of Therapeutic Effect between Combination of Aspirin and Clopidogrel, Clopidogrel Alone, Aspirin 300 mg Alone and Aspirin 100 mg Alone against Functional Outcome and Recurrence in Ischemic Stroke Patients

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Objective: The objective of this study was to compare the efficacy of the aspirin and clopidogrel as combination therapy and single therapy for acute ischemic stroke treatment and its recurrence prevention.

Method: This was an experimental study with double blind randomized pretest-posttest design. The subjects were 48 acute ischemic stroke patients in Adam Malik General Hospital Medan, which divided into 4 groups. Each group consisted of 12 subjects. The first group received combination of aspirin-clopidogrel therapy (aspirin 300 mg and clopidogrel 75 mg), the second group received clopidogrel 75 mg and placebo, the third group received aspirin 300 mg and placebo, and the fourth group received aspirin 100 mg and placebo. Each group consumed the drugs for 1 month since acute phase of stroke. Functional outcome was measured by NIHSS and mRS on thirtieth day after stroke onset. All the subjects clinically followed-up for 1 month to assess any recurrent stroke.

Result: From the 48 subjects included, 29 subjects had good functional outcome by NIHSS measurement without significant differentiation ($p = 0.0120$). We found that 35 subjects had good functional outcome by mRS measurement without significant differentiation ($p = 0.410$). Only 6 subjects had recurrent stroke during follow up {first group (RR 0.32; 95% CI 0.27 to 0.49; $p = 0.070$), second group (RR 0.21; 95% CI 0.18 to 0.28; $p = 0.030$), third group (RR 0.59; 95% CI 0.52 to 0.67; $p = 0.054$), fourth group (RR 0.63; 95% CI 0.57 to 0.70; $p = 0.043$)}.

Conclusion: This study suggest that there were no significant differentiation between combination aspirin and clopidogrel, clopidogrel alone, aspirin 300 mg alone and aspirin 100 mg alone in improving ischemic stroke functional outcome and recurrent stroke prevention.

Topic 05. Neuroimaging Studies

1285

MRI Brain Findings in Elite Singaporean Female Rugby Players before and after Competition

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Objectives: To demonstrate with MRI brain findings in elite contact sports athletes before and after competition.

Methods: Study was cleared by Institution Review Board. Ten female local contact sports athletes were invited for MRI scans 1 week apart, the latter done 4 days after the individuals participated in a competition. All individuals were scanned on a 3T Siemens MAGNETOM Skyra (Siemens Medical Solutions, Erlangen, Germany) with a 32 channel head coil. Structural T1, T2 weighted sequences, diffusion weighted imaging (DWI), susceptibility weighted imaging (SWI), diffusion tensor imaging (DTI) and Magnetic Resonance Spectroscopy (MRS) were performed for all individuals pre and post competition. The post competition MRI scans were compared with the pre competition scans.

Results: All athletes had normal brain structure with no acute infarcts on DWI or haemorrhage on SWI pre and post competition. There was no change in the mean fractional anisotropy in the cerebral white matter pre and post competition. There was no significant change in the right cerebral and left cerebral brain metabolites pre and post competition. There was decreased average NAA to Creatine ratio (NAA/Cr) on MRS of cerebral white matter post competition, with a ratio of 2.15 ± 0.26 pre competition decreasing to 2.01 ± 0.18 post competition ($p < 0.004$). The right cerebral NAA/Cr and left cerebral NAA/Cr ratios showed no significant change post competition.

Conclusions: No acute infarcts, haemorrhage or change in fractional anisotropy is seen in the brains of elite Singaporean female rugby players before and after competition. Although there is minor drop in the average NAA/Cr cerebral white matter post competition which is statistically significant, this is not supported by separate analysis of the right and left cerebral NAA/Cr values.

Topic 06. Neurogenetics

1070

The Clinical Study of Polish Patients with Hereditary Spastic Paraplegias

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Introduction: Hereditary spastic paraplegias (HSP) are a group of clinically and genetically heterogeneous, neurodegenerative disorders characterized by progressive spasticity of the lower limbs. Among autosomal dominantly inherited forms of HSP the most common are SPG4, SPG3 and SPG31, caused by SPAST, ATL1 and REEP1 genes mutations, respectively. The most frequent autosomal recessive form is SPG11. The phenotype may be pure or complex.

Objectives and Methods: In a group of 241 index patients clinically diagnosed as HSP (criteria according to Fink), we identified 15 microrearrangements and 24 point mutations in the SPAST gene, 7 different missense mutations in ATL1 gene, 4 point mutations in the REEP1 gene and 5 deletions in SPG11 gene. Individuals were assessed by Spastic Paraplegia Rating Scale and classification used by Dürr.

Results: Age at onset ranged 1–52, 1–32, 3–17, 10–16 years, disease duration 0–75, 0–80, 0–38, 9–23 years, SPRS scores 0–48, 0–30, 0–20, 42–49 for SPG4, SPG3, SPG31 and SPG11 groups, respectively. All SPG11 patients could not move without walking aids. The majority of patients with SPG4, SPG3 and SPG31 (52%, 76%, 82%) had gait disturbances but did not require aids. Some individuals with SPAST, ATL1 and REEP1 genes mutations (6%, 4%, 9%) didn't complain of gait problems, but neurological examination detected signs of spasticity.

Conclusion: The present study confirmed considerable variability in functional profile among the affected individuals. All patients with mutations in SPG11 gene had severe complex form of HSP. Autosomal dominant SPG forms presented more heterogeneous phenotype. In two SPG3 families (with different mutations) incomplete penetrance was noted.

Topic 07. Neuropharmacology

1160

The Phase I Clinical Study of TMS-007, a Member of the Anti-Inflammatory Thrombolytic SMTP

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Background and Objective: SMTP is a family of small molecules derived from a fungus. SMTP modulates plasminogen conformation and enhances its proteolytic activation, thus promoting endogenous plasmin formation. Along with the thrombolytic activity, SMTP inhibits soluble epoxide inside the cells, leading to anti-inflammatory responses. Based on the two mechanisms, SMTP effectively treats thrombotic and embolic strokes in animal models in rodents and primates. SMTP reduces hemorrhagic transformation and has a wide therapeutic time window. The aim of this project is to develop TMS-007, a promising SMTP congeners, as a drug widely used for stroke patients.

Methods: The standard nonclinical testings were performed according to the ICH guidelines using a GMP grade TMS-007, of which manufacturing methods, specifications, and testing methods were established. Pharmacological studies were performed with various ischemic stroke models in rodents and primates. A randomized, placebo-controlled, double blind phase I study of TMS-007 was performed with healthy male volunteers aged from 20 to 45 years. The study consisted of 5 cohorts differing in the dose from 3 to 360 mg per body by a single intravenous infusion for 30 min.

Results: In embolic stroke models in the mouse, gerbil, and monkey, TMS-007 was efficacious in reducing infarct size and ameliorating neurological deficits with treatment 3–6 h after embolization. In atherothrombotic stroke model in monkeys, TMS-007 suppressed infarct development and hemorrhagic transformation. No obvious toxicity was observed at a pharmacological dose of TMS-007 in the GLP testing. We successfully completed the first-in-human phase I study. The pharmacokinetic parameters as well as adverse events observed were quite similar to those observed with monkeys.

Conclusions: TMS-007 is a promising candidate of a new generation stroke drug.

1286

Sleep Disturbance in Developmental Disorders

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Objectives: In pharmacotherapy for developmental disorders, not only anti-psychotic drugs, a combination of anti-epileptic drugs have an effective for sleep disturbance. Evidence of sleep

disturbance in developmental disorders associated with abnormal EEG has not been established. We evaluated the EEG abnormalities and usefulness of anti-epileptic drugs for sleep disturbance in developmental disorders.

Methods: A total of 150 children (110 boys, 40 girls, mean 12.7 years) were included in this study. EEG had been recorded every 6 months under sleep conditions. We examined the therapeutic effect of behavioral and psychiatric improvement and sleep disturbance.

Results: EEG abnormalities were present in 76.7%, sleep disturbance was complicated in 33.3% of whole; 41.4% in autism spectrum disorders and 16.4% in attention deficit hyperactivity disorders respectively. Epilepsy was present in 53.3%. Almost patients showed EEG abnormalities on frontal areas. Although, there is no statistically difference in the effectiveness of anti-psychotic drugs or anti-epileptic drugs, all patients in the both combined patients were more improved.

Conclusions: Anti-epileptic drug is effective for sleep disturbance in developmental disorders who showed EEG abnormalities. In cases of EEG abnormalities, anti-epileptic drugs may be an alternative treatment for sleep disturbance in developmental disorders.

Topic 08. Neuropsychiatry

1284

Repetitive Transcranial Magnetic Stimulation in Anxiety and Depression

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Objective: Treatment resistant depression (TRD) is common, and Electroconvulsive Therapy (ECT) remains the gold standard for TRD; however, it does not alleviate anxiety. We present the case of a gentleman with chronic TRD and social anxiety, who failed ECT and left sided repetitive transcranial magnetic stimulation (rTMS) but then responded to right sided rTMS.

Methods: The patient is a 44 year old married mixed race male, with a history of chronic major depressive disorder, dysthymic disorder and social anxiety who is otherwise healthy. He had adequate trials of multiple psychotropic medications and psychotherapy. Right unilateral ECT was initiated, but after six sessions without any response, he was switched to bilateral ECT for a total of twenty sessions after which it was discontinued due to lack of clinical benefit. He thus began left unilateral, high frequency (10 Hz) rTMS.

Results: Using the Montgomery-Asberg Depression Rating Scale (MADRS), his initial score was 24. In total, the patient received 32 left sided treatments; however, he failed to respond. He was switched to right sided rTMS and after 20 sessions his MADRS score decreased to 9. He has been continued on maintenance rTMS therapy and remains in remission.

Conclusions: To date, there have been no reported cases of TRD and comorbid anxiety with response to treatment with low frequency, right sided rTMS after first failing both ECT and left, high frequency rTMS. This case illustrates that rTMS is emerging as a treatment option for TRD and anxiety and may play a crucial role in providing relief to those patients who suffer with both depression and anxiety. If the more commonly practiced left sided, high frequency rTMS proves ineffective, then right sided, low frequency treatment should be considered. Patients with TRD may be also suffering from anxiety, which, if alleviated, may help improve their depression.

Topic 09. Public Health

1276

Pregnane Isomers Are Increased in Female Patients with Multiple Sclerosis

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Multiple sclerosis (MS) is one of the most common neurological disorders. It is a demyelinating autoimmune disease which leads to disability in humans. Currently, the sex ratio females : males is approaching 3: 1. It is known that the neuroactive steroids (NAS) exert local effects on glial and neuronal tissue. Some NAS prevent or reduce neurodegeneration. The objective of the study was to compare serum levels of neuroactive steroids in female patients with MS and healthy controls.

We have followed serum GABAergic, glycinergic, glutamatergic, acetylcholinergic and purinergic NAS, their precursors and metabolites and their conjugates (64 steroids) of 13 female patients (36 years old median age) and 5 sex age matched healthy controls (both in the follicular menstrual phase) with the use of gas chromatography – mass spectrometry. Relationships between dependent variables were evaluated using the age-adjusted ANOVA model consisting of the Status (patients with MS vs. controls) factor. To eliminate skewed data distribution and heteroscedasticity, the original data were transformed by a power transformation to attain Gaussian distribution and constant variance before further processing.

Our study reveals increased levels of C21 steroids (including allopregnanolone) in the serum of female patients with MS.

This finding suggests increased activity of adrenal glands as mechanism enabling a consequent synthesis of neuroprotective steroids in various peripheral tissues.

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Erratum

One of the abstracts of the '5th International Conference on Neurology and Epidemiology, Gold Coast, Australia, November 18–20, 2015' [Neuroepidemiology 2015;45:298–337, DOI: 10.1159/000441544] was erroneously not published. Please find it below.

Poster Presentation

Topic 12. Basics and Translation

1289

Hyperglycemia Decreases the Expression of Astrocytic Phosphoprotein PEA-15 and Its Two Phosphorylated Forms in the Brain after Cerebral Ischemia

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Stroke is a serious cerebrovascular disorder and a major cause of death. Diabetes mellitus is a metabolic disorder that strongly increases the risk of severe vascular diseases. Phosphoprotein enriched in astrocytes 15 (PEA-15) is known to modulate various cellular processes including cell proliferation, apoptosis, and survival. In this study, it was investigated whether hyperglycemic condition modulates the levels of PEA-15 and its two phosphorylated forms (Ser 104 and Ser 116) in a cerebral ischemic injury model. Adult male rats were injected with streptozotocin (40 mg/kg) via the intraperitoneal route to induce diabetes and underwent surgical middle cerebral artery occlusion (MCAO) 4 weeks after streptozotocin treatment. A decrease in the PEA-15 level after ischemic injury was detected using a proteomic approach. Moreover, PEA-15 protein expression was reduced to a greater extent in diabetic animals than in non-diabetic animals. Western blot analysis clearly confirmed that hyperglycemic condition exacerbates the decrease in PEA-15 and phospho-PEA-15 (Ser 104 and Ser 116) proteins after MCAO. The decrease in the phospho-PEA-15 protein level indicates that the anti-apoptotic function of PEA-15 was inhibited. Thus, these results suggest that the diabetic condition may exacerbate brain damage during focal cerebral ischemia through downregulation of PEA-15 and phospho-PEA-15 proteins. This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MEST) (NRF-2013R1A1A2007300).