



MEETING ABSTRACTS

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# Abstracts from Hydrocephalus 2015

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## INTRODUCTION

I1

### Hydrocephalus 2015, The 7<sup>th</sup> Annual Meeting of the International Society for Hydrocephalus and CSF Disorders (ISHCSF)

Mark Hamilton

Department of Clinical Neurosciences University of Calgary, Division of Neurosurgery, Foothills Hospital, 12th Floor, 1403 - 29th Street NW, Calgary, AB Canada T2N 2T9

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The 7<sup>th</sup> Annual Meeting of the International Society for hydrocephalus and Cerebrospinal Fluid Disorders (ISHCSF) is being held in Banff, Alberta, Canada September 19<sup>th</sup>-21<sup>st</sup>, 2015.

There are three satellite symposia accompanying the main Congress. On September 17<sup>th</sup>, the **1<sup>st</sup> Calgary Hydrocephalus Symposium** will be hosted by the Cumming School of Medicine to provide an intimate opportunity to explore state-of-the-art hydrocephalus care. On September 18<sup>th</sup>, the satellite **Normal Pressure Hydrocephalus (NPH) Symposium** will be held in Banff, providing an opportunity to share and learn from the experience of international experts regarding this challenging hydrocephalus disorder. We also welcome our colleagues and members of the **International Hydrocephalus Imaging Working Group (IHIWG)**. IHIWG members include Neurologists, Neurosurgeons, Neuroradiologists and Physicists who will have their autumn meeting on September 18<sup>th</sup> in Banff.

**Hydrocephalus 2015** will cover the full range of CSF disorders affecting both children and adults. The focus of work done in our field is the patient and to this end, the theme of three special sessions of this Congress will be **"The Patient"**. These special sessions will examine: 1) Quality Improvement and Safety in Hydrocephalus Care; 2) Transition and Adult Hydrocephalus Care; and 3) Ethics and Patient Involvement in Clinical Research. These sessions will provide a foundation for the research that will be presented during **Hydrocephalus 2015** which will include sessions dealing with pediatric hydrocephalus, adult hydrocephalus, advanced Neuro-imaging techniques in hydrocephalus, CSF shunt design and technology and intracranial pressure. We will also have special sessions devoted to young investigators and will recognize those with the best oral presentations and best posters.

We have a great social program to span the conference. We start with the Welcoming Reception on September 18<sup>th</sup>, party at a bar-be-que buffet barn dance on September 19<sup>th</sup> and then celebrate at the Denim and Diamonds Gala Dinner on September 20<sup>th</sup>. Our very special guest speaker for the Gala Dinner is Dr. Michael Bliss, renowned historian and author of "Harvey Cushing. A Life in Surgery".

## ORAL PRESENTATIONS

O1

### Trends in hospitalization of preterm infants with intraventricular hemorrhage and hydrocephalus in the United States, 2000-2010

Eisha Anne Christian<sup>1\*</sup>, Diana Jin<sup>1</sup>, Frank Attenello<sup>1</sup>, Timothy Wen<sup>1</sup>, Steven Cen<sup>1</sup>, William J Mack<sup>1</sup>, Mark D Krieger<sup>1,2</sup>, J Gordon McComb<sup>1,2</sup>

<sup>1</sup>University of Southern California, Los Angeles, CA, USA; <sup>2</sup>Children's Hospital Los Angeles, CA, USA

E-mail: [echristi@usc.edu](mailto:echristi@usc.edu)

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**Objective:** Even with improved prenatal and neonatal care, intraventricular hemorrhage (IVH) occurs in approximately 25-30% of preterm infants, and a subset of these patients develop hydrocephalus. We aim to describe current trends in hospitalization of preterm infants with IVH and post-hemorrhagic hydrocephalus (PHH) using the Nationwide Inpatient Sample (NIS) and Kids Inpatient Database (KID).

**Methods:** The KID and NIS databases were combined to generate data for the years 2000 - 2010. All neonatal discharges with ICD9-CM codes for preterm birth with IVH alone or with IVH and hydrocephalus were included.

**Results:** There were 147,823 preterm neonates with IVH, and 9% of this group developed hydrocephalus during the same admission. Twenty-five percent and 28% of patients with Grades 3 and 4 IVH respectively developed hydrocephalus in comparison to 1% and 4% of patients with Grades 1 and 2 IVH. Thirty-eight percent of patients with PHH had permanent ventricular shunts inserted. Mortality rates were 4%, 10%, 18%, and 40% respectively for Grades 1-4 during initial hospitalization. Length of stay has been trending upward for both groups of IVH (49d in 2000, 56d in 2010) and PHH (59d in 2000, 70d in 2010). Average hospital cost per patient (inflation-adjusted) has also increased from \$201,578 to \$353,554 (IVH) and \$260,077 to \$495,697 (PHH) over 11 years.

**Conclusion:** The number of admissions of neonates with IVH has increased despite a decrease in the number of preterm births. Rates of hydrocephalus and mortality correlated closely with IVH grade. Incidence of hydrocephalus in preterm infants with IVH remained stable between 8-10%. Over an 11-year period, there was a progressive increase in hospital cost and length of stay for preterm neonates with IVH and PHH with a concurrent increase in the proportion of patients with congenital cardiac anomalies.

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## O2

### Hardware-in-the-loop testing of CSF shunts

Manuel Gehlen<sup>1,2\*</sup>, Vartan Kurtcuoglu<sup>2</sup>, Marianne Schmid Daners<sup>1</sup>

<sup>1</sup>Department of Mechanical and Process Engineering, ETH Zurich, Switzerland; <sup>2</sup>Institute of Physiology, University of Zurich, Switzerland  
E-mail: mgehlen@ethz.ch

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**Introduction:** Siphoning in upright posture has led to a multitude of increasingly complex cerebrospinal fluid (CSF) shunts. These shunts use a diversity of approaches to solve the problem of the resulting overdrainage. Overdrainage and the generally high failure rate of CSF shunts have led to the vision of an actively controlled shunt that adapts its drainage rate to the needs of the patient. This evolution towards more complex devices calls for fast and cost-effective in vitro testing methods that provide information on the interaction of shunt and the patient's CSF system.

**Methods:** We designed a hardware-in-the-loop (HIL) test bed that provides this information by adapting the tested shunt's environment according to a real-time simulation of the patient. A mathematical model of the patient's relevant pathophysiology simulates the influence of the measured drainage through the shunt, the patient's posture, and cardiac-induced pulsations on intracranial and intraperitoneal pressure. These pressures are then applied to the proximal and distal catheter tips of the CSF shunt through highly dynamic pressure interfaces. As the posture of the simulated patient changes, the tested shunt is moved accordingly by a posture mechanism with two degrees of freedom. The resulting CSF drainage through the shunt is measured and fed back to the patient simulation in real-time.

**Results:** During experiments with this HIL test bed and standard differential pressure valves we were able to replicate the problem of overdrainage: Within  $9.2 \pm 1.5$  min after sitting up, mean ICP fell to  $-21.1 \pm 1.3$  mmHg relative to the external auditory canal due to drainage rates of up to  $4.4 \pm 0.2$  mL/min. Avoidance of this overdrainage through the addition of a gravitational unit was also reproduced, with mean ICP in sitting position only falling to  $-9.1 \pm 0.1$  mmHg. The experiments further revealed that the pressure interfaces can reproduce even pulsatile ICP signals with less than 0.1 mmHg mean absolute error, allowing the application and analysis of any pathophysiological pulse pressure waveform. Using a 24-hour test cycle based on measured patient data allowed us to compare shunts during typical daily activities.

**Conclusion:** The experiments showed that HIL testing can be used to accurately analyze and quantify the dynamic interaction between shunt and patient in a realistic yet reproducible in vitro environment. By virtue of the realistic implementation of this interaction, the results will also be valid for actively controlled shunts, which adapt to measured parameters of the patient's pathophysiology. We thus see our test bed as a catalyst for the development of future shunt systems by enabling fast and cost-effective testing of new ideas and concepts, while reducing animal trials.

## O3

### Morphological changes in ICP pulse waveform as potential markers for early determination of external ventricular drain clamping trial outcome

Jorge Arroyo Palacios<sup>1\*</sup>, Maryna Rudz<sup>1</sup>, Richard Fidler<sup>1</sup>, Wade Smith<sup>1</sup>, Nerissa Ko<sup>1</sup>, Marvin Bergsneider<sup>2</sup>, Xiao Hu<sup>1</sup>

<sup>1</sup>University of California, San Francisco, USA; <sup>2</sup>University of California, Los Angeles, USA

E-mail: jorge.arroyopalacios@ucsf.edu

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External ventricular drains (EVD) are widely used to measure and manage intracranial pressure (ICP) for aneurysmal subarachnoid hemorrhage (aSAH) patients. After several days of use a decision is made to remove the drain or replace it with an indwelling shunt. This involves a "clamping trial" whereby the EVD is clamped and transduced and pre and post clamping CT imaging is performed to observe any change in ventricular size and clinical status. This practice may lead to prolonged hospital stay, extra radiation exposure, and neurological insult. The present study aims to apply a widely validated morphological clustering analysis of ICP pulse (MOCAIP) algorithm to detect signatures from the pulse waveform to differentiate an intact CSF circulatory system from an abnormal one during EVD clamping. We hypothesize that an intact CSF system should be stable and pulses with a similar mean ICP level should have similar shapes.

This is a retrospective study with 43 out of 107 adult patients that satisfied the inclusion criteria of ICD9 code for SAH, admitted to UCSF Medical Center between 03/2013 and 08/2014, and exclusion criteria of absence of reported EVD clamping trial and ICP signal recordings shorter than 2 hours. By reviewing the clinical notes and pre/post brain imaging results, 25 patients were determined with an intact CSF circulatory system (group A) and 18 patients with an impaired one (group B). Blind to the chart review, the MOCAIP algorithm was applied to the ICP signal recordings to form a series of artifact-free dominant pulses. Then, for each pulse, other pulses with similar mean ICP were identified. Finally, the Euclidean and geodesic inter-pulse distances were calculated in a 4 hours moving window.

ANOVA analyses showed a significant difference on the standard deviations of the Euclidean ( $p < 0.001$ ,  $\eta^2 = 0.29$ ) and geodesic distance ( $p = 0.001$ ,  $\eta^2 = 0.22$ ), between groups A and B. Mann-Whitney U tests were used on the (non-normally distributed) mean distances, showing a significant difference on the Euclidean ( $p = 0.007$ ,  $r = 0.41$ ) and the geodesic distance ( $p = 0.02$ ,  $r = 0.36$ ) between the two groups of patients. The area under the ROC curve was 0.79 and 0.78 for the standard deviations of the Euclidean and geodesic distance, and 0.74 and 0.71 for the mean Euclidean and geodesic distance respectively.

Patients with an impaired CSF system showed not only a larger mean but also a larger variability of the inter-pulse distances, indicating frequent changes on the morphology of the pulses. The variability of morphological distances was the best predictor of the effect of EVD clamping trial. This technique may provide a method to rapidly determine if a patient will need surgical placement of an indwelling shunt or can simply have the EVD removed following SAH.

## O4

### Association between apathy and regional cerebral blood flow in patients with idiopathic normal pressure hydrocephalus

Hideki Kanemoto<sup>\*</sup>, Hiroaki Kazui, Takashi Suehiro, Shingo Azuma, Syunsuke Sato, Yukiko Suzuki, Kenji Yoshiyama

Department of Psychiatry Osaka University Graduate School of Medicine, Japan

E-mail: hkanemoto0427@gmail.com

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**Introduction:** Apathy is a common symptom in idiopathic normal pressure hydrocephalus (iNPH). However, the neuroanatomical bases of apathy in iNPH has not been well examined. We assessed the relationship between improvement of apathy and change of regional cerebral blood flow (rCBF) after shunt surgery.

**Methods:** We recruited 20 iNPH patients who had apathy before shunt surgery. They were tested about apathy with Neuropsychiatric Inventory (NPI) and cognitive function with Mini-mental State Examination (MMSE) and Frontal Assessment Battery (FAB). They were also evaluated quantitative rCBFs of 32 regions-of-interests (ROIs) with 123I-HMP single photon emission computed tomography (SPECT) using the autoradiography method. All the evaluations were conducted both before and 3 months after shunt surgery. They were classified into two subgroups; one was improved apathy (APA+) and another was not (APA-). The changes of rCBFs after the shunt were evaluated in each subgroup, respectively. In addition, we assessed the correlations between the changes of apathy and cognitive functions after shunt surgery.

**Results:** Ten patients categorized in APA+ group. In APA+ group, rCBFs in 3 ROIs, bilateral anterior cingulate cortices (ACC) and right caudate

nucleus, were significantly improved after shunt surgery. In APA-group, rCBFs in 2 ROIs, splenium of corpus callosum and right amygdala, were significantly improved after shunt surgery. A significant correlation was found between the changes of apathy score in NPI and score of FAB.

**Conclusions:** Dysfunction of bilateral ACC and right caudate nucleus could cause apathy, and severity of apathy could be correlated with frontal dysfunction in iNPH. Caudate is known as a key structure of apathy related to disruption of cognitive processing. The results in the present study might indicate that iNPH led to apathy as a result of frontal dysfunction due to caudate impairment.

## O5

### Cerebral microbleeds in idiopathic normal pressure hydrocephalus

Elias Johansson<sup>1\*</sup>, Khalid Ambaraki<sup>2,3</sup>, Richard Birgander<sup>2</sup>, Nazila Bahrami<sup>2</sup>, Anders Eklund<sup>2,3</sup>, Jan Malm<sup>1</sup>

<sup>1</sup>Department of Pharmacology and Clinical Neuroscience, Umeå University, Sweden; <sup>2</sup>Department of Radiation Sciences, Umeå University, Sweden; <sup>3</sup>Centre for Biomedical Engineering and Physics, Umeå University, Sweden  
E-mail: elias.johansson@umu.se

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**Introduction:** Cerebral microbleeds (CMB) have been associated with dementia and small vessel disease, which also are features in idiopathic normal pressure hydrocephalus (iNPH). This study aims to analyze if CMB are associated with iNPH.

**Methods:** Case-control study. We included 14 patients with iNPH (mean age 76 years, 60% female) and 41 healthy controls (HeCo; mean age 71 years, 60% female). All were investigated with magnetic resonance imaging using a T2\*-sequence. After investigation, iNPH patients underwent shunt surgery. We compared the presence of  $\geq 2$  CMB between the cases and controls.

**Results:**  $\geq 2$  CMB were detected more frequently in the iNPH group compared to HeCo (n=6, 43% versus n=4, 10%; p=0.01). Among the participants with CMB, the number of CMB was higher among the iNPH patients than the HeCo (median 8; IQR 2-34 versus median 1; IQR 1-2; p=0.005). Two cases died within 30 days post-operatively; these had the highest number of microbleeds in the cohort (34 and 174 CMB).

**Conclusion:** The prevalence of CMB seems to be increased in patients with iNPH. The results may support a vascular component as a part of the iNPH pathophysiology. The possible association between CMB and poor outcome warrants further study.

## O6

### Deformation, microstructure and stiffness of the rat brain tissue during the development of experimental obstructive hydrocephalus

Lauriane Jugé<sup>1\*</sup>, Alice Pong<sup>2</sup>, Andre Bongers<sup>3</sup>, Ralph Sinkus<sup>4</sup>, Lynne E Bilston<sup>1</sup>, Shaokoon Cheng<sup>5</sup>

<sup>1</sup>Neuroscience Research Australia, University of New South Wales, Australia; <sup>2</sup>Neuroscience Research Australia, Australia; <sup>3</sup>University of New South Wales, Australia; <sup>4</sup>King's College London, UK; <sup>5</sup>Neuroscience Research Australia, Macquarie University, Australia  
E-mail: l.juge@neura.edu.au

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**Introduction:** Understanding neural injury in hydrocephalus and how key physiological factors changes during the course of the disease in-vivo remain unclear. This study aims to describe brain deformation, microstructural and mechanical properties changes during obstructive hydrocephalus (HCP) development in a rat model using multimodal magnetic resonance (MR) imaging.

**Methods:** Hydrocephalus was induced in 8 Sprague-Dawley rats by injecting a kaolin suspension into the cisterna magna. 6 sham-injected rats were used as controls. MR imaging (9.4T, Bruker) was performed 1 day before, then at 3, 7 and 16 days post injection. T2-weighted MR images were collected to quantify ventricular enlargement and brain deformation. MR elastography was used to measure the brain stiffness, and diffusion tensor imaging (DTI) was conducted to observe brain tissue microstructure. Histology examination was performed immediately after the last MR scan. Generalized estimating equations (GEE) were used to assess linear relationships between variables while accounting for repeated measure design.

**Results:** The enlargement of the ventricular system was associated with a decrease in the cortical gray matter thickness and basal ganglia cross-sectional area from day 3 (P<.001, for both), an alteration of the corpus callosum microstructure and rearrangement for the cortical gray matter microstructure (P<.001, for both), while a compression without gross microstructural alteration was evident for the basal ganglia and internal capsule (P<.001, for both), not seen in controls. Specifically, during hydrocephalus development, increase in space between the white matter tracts was observed in the corpus callosum (P<.001), while a decrease of space was observed for the internal (P<.001). For the cortical gray matter, an increase in extracellular tissue water originating from the ventricles via the discontinuous ependyma was observed and significantly associated with a decrease in stiffness (P=.001). Finally, for the basal ganglia, results suggested a progressive compression of the tissue, beginning with the periventricular region, then extending to the entire structure. The basal ganglia did not appear to be edematous, and the tissue compression was associated with an increase in stiffness (P=.001).

**Conclusions:** This study outlines the temporal changes in tissue microstructure, water content and stiffness in different brain regions using DTI and MR elastography and how these changes are associated with ventricular enlargement. It shows that the effect of ventricular enlargement is not limited to periventricular white matter, severity of microstructural changes vary with brain region and there is regional and temporal variation in brain tissue stiffness during hydrocephalus development.

## O7

### Mortality and dementia in untreated iNPH: a 25-year follow-up of a population-based cohort

Daniel Jaraj<sup>1\*</sup>, Katrin Rabiei<sup>1</sup>, Thomas Marlow<sup>1</sup>, Christer Jensen<sup>2</sup>, Ingemar Skoog<sup>1</sup>, Carsten Wikkelsø<sup>1</sup>

<sup>1</sup>Inst of Neuroscience and Physiology, University of Gothenburg, Sweden; <sup>2</sup>Inst of Clinical Sciences, University of Gothenburg, Sweden  
E-mail: daniel.jaraj@gmail.com

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**Introduction:** We examined mortality and risk of dementia in persons with untreated possible and probable iNPH using a large, prospective population-based cohort.

**Methods:** 1235 persons aged 70 years or more were included. Baseline examinations, including CT of the brain, were made between 1986 and 2000. Cases were diagnosed using criteria from international consensus guidelines and were followed until 2012. A total of 53 persons had radiological features compatible with iNPH. Of these, 24 fulfilled criteria for probable iNPH, while 29 were asymptomatic or had possible iNPH. None of the cases had been treated with shunt. Outcome data was obtained from clinical examinations, the Swedish Hospital Discharge Register and the National Swedish Death Registry. Risks were compared using Cox proportional hazard regression.

**Results:** Median follow-up time was 11.5 years (Maximum 25 years). Crude 5-year mortality was 88.5 % in those with probable iNPH (n=24), and 19.1 % in those without iNPH (p<0.001). Adjusting for age, sex and cohort, mortality was increased throughout follow-up among persons with probable iNPH (Hazard Ratio 3.8; 95% CI: 2.5-6.0). Main causes of death were cardiovascular disorders. Among those with possible iNPH and asymptomatic radiological iNPH (n=29), who did not have dementia at baseline, 40 % developed dementia during follow-up (Hazard Ratio 2.6; 95% CI: 1.3-5.1).

**Conclusions:** The risk of mortality is substantially increased in those with untreated iNPH. Our findings indicate that persons with radiological features of iNPH have an increased risk of dementia even if they do not fulfill the current clinical criteria for probable iNPH.

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## O8

### Endoscopic third ventriculostomy (ETV) for treatment of adult hydrocephalus: long-term followup with 163 patients

Albert Isaacs<sup>\*</sup>, Geberth Urbaneja, Mark Hamilton  
University of Calgary, Canada  
E-mail: akm.isaacs@gmail.com

Fluids and Barriers of the CNS 2015, 12(Suppl 1):O8

**Introduction:** Treatment of specific patterns of symptomatic hydrocephalus in the adult patient may be accomplished with endoscopic third ventriculostomy (ETV) as an alternative to insertion of a ventriculoperitoneal (VP) shunt or when VP shunt failure occurs. Treatment of hydrocephalus with a VP shunt, while effective, is associated with a significant shunt failure rate that results in VP shunt revision surgery. This review examines a single center experience with ETV to treat hydrocephalus in symptomatic adult patients.

**Methods:** Adult patients (>=18 years) with a diagnosis of hydrocephalus who were treated with ETV in Calgary between January 1994 and July 2014 were reviewed using a clinic database and registry. All patients were treated by one neurosurgeon.

**Results:** 163 adult patients with symptomatic hydrocephalus treated with ETV were identified (male=92; female=71). Mean age at the time of ETV was 46 years (range 18-83 years). 112 underwent ETV as a primary treatment and 51 patients underwent treatment after presenting with VP shunt failure (secondary ETV). 113/163 patients had a diagnosis of aqueductal stenosis, 22/163 had a diagnosis of tumor. Mean followup was 8.2 years (range 0.3-18.4 years). Symptoms in 149/163 (91.4%) of ETV patients were better or unchanged at last followup. 104/118 (88.1%) of primary ETV patients were shunt free at last followup. 39/45 (86.7%) of secondary ETV patients were shunt free at last followup.

**Conclusions:** Endoscopic (ETV) treatment of hydrocephalus is an effective longterm treatment in a select population adult patients with hydrocephalus. Outcome/results are similar for patients where ETV is used as either a primary or secondary treatment. 87-88% of patients remain shunt free with a mean 8.2 years of followup.

**Learning objectives:** 1) To understand the role of ETV for primary treatment of hydrocephalus in the adult patient.

2) To understand the role of ETV for secondary treatment of hydrocephalus in the adult patient.

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## O9

### Impact of antibiotic-impregnated catheters on the reduction in operations for cerebrospinal fluid shunt infection since 1995: evidence from the UK Shunt Registry

John D Pickard<sup>\*</sup>, Hugh K Richards, Helen M Seeley

University of Cambridge, UK

E-mail: jdp1000@cam.ac.uk

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**Introduction:** Various methods have been introduced to reduce CSF shunt infection including institutional protocols, antibiotic prophylaxis and antibiotic-impregnated catheters. Have such measures led to a sustainable reduction in CSF shunt infections?

**Methods:** The United Kingdom Shunt Registry is a paper-based reporting system for CSF shunts inserted in the 34 UK neurosurgery units since May 1995. This Report is based on data downloaded on 23rd January 2015 from the master database that gave a shunt procedure dataset from 1st January 1995 to 31st December 2014 of 53,767 procedures in 29,341 patients. The infection risk was calculated as the proportion of procedures subsequently revised for infection based on "intention to treat" recorded at the time of surgery where the follow-up was greater than nine months. Subsequent bacteriological confirmation was not available.

**Results:** There was a trend towards a fall in shunt infection risk in both adults and children over recent years. With regard to the impact of the

introduction of antibiotic-impregnated catheters, our previously published study was based on a cohort of 994 pairs matched for age, diagnosis, number of previous procedures and gender procedures recruited up until the end of 2006. The infection risk in that cohort was reduced from 4.7% using conventional catheters to 3.0% using Bactiseal catheters. Data from 2007 onwards was used to construct a second matched-pair comparison. 11938 procedures were identified where patients could be defined by age, diagnosis gender and number of previous revisions. 6302 antibiotic-impregnated catheters and 5636 conventional catheters were used. This data set yielded 4011 matched pairs. The calculated infection risk was 1.87% in conventional catheters and 1.12% in antibiotic-impregnated catheters (p=0.006).

**Conclusions:** The overall risk of shunt infection at all ages has reduced over recent years. Antibiotic-impregnated catheters have significantly reduced shunt infections but other factors may have played a role.

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## O10

### Attitudes regarding endoscopic third ventriculostomy and choroid plexus coagulation (ETV+CPC) and the effect of training at CURE Children's Hospital, Uganda among North American pediatric neurosurgeons

Jay Riva-Cambrin<sup>1\*</sup>, Heather Spader<sup>1</sup>, Abhaya Kulkarni<sup>2</sup>, Benjamin Warf<sup>3</sup>,

John Mugamba<sup>4</sup>, Peter Ssenyonga<sup>4</sup>

<sup>1</sup>University of Utah, USA; <sup>2</sup>University of Toronto, Canada; <sup>3</sup>Harvard University,

USA; <sup>4</sup>CURE Hospital, Uganda

E-mail: jay.riva-cambrin@hsc.utah.edu

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**Introduction:** The ETV+CPC technique has permeated from CURE Hospital in Uganda to North America and neurosurgeons have travelled to Uganda to learn the nuances of this technique. The goal of this study was to determine current attitudes of North American pediatric neurosurgeons towards ETV+CPC and the effects of training at CURE on attitude and clinical practice.

**Methods:** The electronic cross-sectional survey comprised of general questions and specific cases examining practices and attitudes regarding shunts, ETV, and ETV+CPC for the management of infant hydrocephalus. Twelve surgeons were identified as having trained at CURE and each surgeon was matched with 4 other pediatric neurosurgeons based on length of practice. The CURE-trained neurosurgeons were asked about their ETV+CPC attitudes and management before and after training.

**Results:** Overall response rate was 67% (37/55). Of all respondents, 41% thought ETV+CPC was superior to CSF shunting, 24% thought it was inferior, and 8% felt they were equivalent. Of the CURE trainees, 38% did

not offer ETV+CPC and only 16% used ETV+CPC  $\geq 25\%$  of the time before training. After training in Uganda, the percentage of surgeons who thought ETV+CPC was superior doubled (80% vs. 40%,  $p=0.2$ ) and the trained surgeons offered ETV+CPC more often as 70% of them now offer ETV+CPC use  $\geq 50\%$  of the time compared to 0% pre-training ( $p=0.012$ ).

**Conclusion:** For the treatment of infant hydrocephalus, there appears to be equipoise regarding the preference of ETV+CPC versus shunt. Training at CURE led to more favorable attitudes and an increased propensity to offer ETV+CPC.

## O11

### The role of hypertension and diabetes mellitus in the severity of gait and balance disturbances in iNPH

Simon Agerskov<sup>\*</sup>, Maria Wallin, Per Hellström, Carsten Wikkelso, Mats Tullberg  
Hydrocephalus research unit at the institute of neuroscience and physiology, the Sahlgrenska Academy at the University of Gothenburg, Sweden  
E-mail: si.agerskov@gmail.com

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**Background:** Idiopathic normal pressure hydrocephalus (iNPH) is a disorder characterized by gait and balance disturbances, urinary incontinence and cognitive impairment. Of these three, gait and balance disorders are often the first to manifest and also the group that improve the most after shunt surgery. Vascular risk factors (particularly hypertension and diabetes mellitus) has been shown to increase the risk of developing iNPH. There is however further need to investigate if these risk factors have any impact on the severity of symptoms and improvement after shunt surgery.

The aim of this study is to examine the connection between hypertension, diabetes mellitus (DM) and the severity of gait and balance disturbances in patients diagnosed with iNPH pre- and postoperatively. The aim was also to determine if patients with risk factors present show less improvement in gait and balance after surgery compared to controls.

**Methods:** A local database containing clinical data on all iNPH-patients diagnosed and treated in Gothenburg between 1978 and 2013 was used. The database contains a total of 389 patients diagnosed in accordance with the American-European guidelines. Gait and balance were measured using: a seven step scale (higher score indicating a more severe disturbance), the Romberg test, TUG-test and the 10m walking test. All tests were performed and recorded by physiotherapists with a special interest in iNPH. Hypertension and diabetes was defined in accordance with the ICD coding system. Differences between groups were tested using the Mann-Whitney U test.

**Results:** Patients who had a documented history of hypertension scored significantly higher on the gait scale (mean score: 3.14 vs 2.65,  $p<0.001$ ) and also performed worse on all the measured tests. Patients with DM also scored higher on the grading scale (mean: 3.26 vs 2.78,  $p=0.006$ ) and performed worse on the majority of tests compared to controls. After shunt surgery, patients with hypertension or DM still performed at a significantly lower levels compared to controls but did not show a worse relative improvement in gait and balance on the grading scale nor on other tests. The results are preliminary and will be expanded.

**Conclusions:** The presence of hypertension and/or diabetes mellitus not only seems to increase the risk of developing iNPH but seem to accelerate the progression of symptoms. Patients who have either hypertension or DM perform significantly worse in test measuring gait and balance compared to controls before and after shunt surgery. The existence of cardiovascular risk factors does not however, seem to impact the postoperative relative improvement in gait and balance after shunt surgery.

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## O12

### The Wisconsin Hydrocephalus Survey: shunt-dependent hydrocephalus management style among members of the American Society of Pediatric Neurosurgeons

Mark Richard Kraemer<sup>\*</sup>, Bermans J Iskandar  
Department of Neurological Surgery, University of Wisconsin School of Medicine and Public Health, USA  
E-mail: mrkraemer@wisc.edu

Fluids and Barriers of the CNS 2015, 12(Suppl 1):O12

**Introduction:** This survey sought to evaluate differences in the understanding and management of shunt-dependent hydrocephalus among the senior North American Pediatric Neurosurgery membership.

**Methods:** Surveys were sent to all active American Society of Pediatric Neurosurgeons (ASPN) members from September to November 2014. A total of 204 surveys were sent from which 130 responses were recorded, representing 64% of active ASPN membership. Respondents were asked 13 multiple choice and free response questions focusing on four problems encountered in shunted hydrocephalus management: Shunt malfunction, cerebrospinal fluid (CSF) overdrainage, chronic headaches and slit ventricle syndrome (SVS). Qualtrics<sup>®</sup> online survey software was used to distribute and collect response data.

**Results:** ASPN surgeons prefer three varieties of shunt valves: 41% differential pressure, 29% differential with anti-siphon device (ASD), and 27% programmable. Respondents agree shunt obstruction occurs most often at the ventricular catheter due to either in-growth of the choroid plexus (67%), CSF debris (18%), ventricular collapse (8%), or other reasons (9%). Underlying causes of obstruction were attributed to small ventricular size, catheter position, choroid plexus migration, build-up of cellular debris, inflammatory processes, or CSF overdrainage. The majority of respondents (>85%) consider chronic overdrainage a rare complication. These cases are most often managed with ASDs or programmable valves. Chronic headaches are most often attributed to medical reasons (e.g. migraines, tension) and managed with patient reassurance. The most popular treatments for SVS include shunt revision (88%), cranial expansion (57%) and placement of an ASD (53%). SVS etiology was most often linked to early onset of shunting, chronic overdrainage and/or loss of brain compliance.

**Conclusions:** This survey shows discrepancies in shunt-dependent hydrocephalus understanding and management style among a representative group of experienced North American pediatric neurosurgeons. In particular, there are differing opinions regarding the primary cause of ventricular shunt obstructions and the origins of SVS. However, there appears to be general consensus in approach and management of overdrainage and chronic headaches. These results provide impetus for better studies evaluating the pathophysiology and prevention of shunt obstruction and SVS.

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## O13

### Asymptomatic ventricular dilatation precedes clinical decline in rodent adult chronic communicating hydrocephalus

Ignacio Jusue-Torres<sup>1\*</sup>, Jennifer Lu<sup>1</sup>, Eric W Sankey<sup>1</sup>, Tito Vivas-Buitrago<sup>1</sup>, Joshua Crawford<sup>2</sup>, Mikhail Pletnikov<sup>2</sup>, Jiadi Xu<sup>3</sup>, Ari Blitz<sup>4</sup>, Barbara Crain<sup>5</sup>, Alicia Hulbert<sup>6</sup>, Hugo Guerrero-Cazares<sup>1</sup>, Oscar Gonzalez-Perez<sup>7</sup>, Alfredo Quiñones-Hinojosa<sup>1</sup>, Pat McAllister<sup>8</sup>, Daniele Rigamonti<sup>1</sup>  
<sup>1</sup>Johns Hopkins University, School of Medicine, Department of Neurosurgery, USA; <sup>2</sup>Johns Hopkins University, School of Medicine, Department of Psychiatry and Behavioral Sciences, USA; <sup>3</sup>Johns Hopkins University, School of Medicine, F. M. Kirby Research Center for Functional Brain Imaging at the Kennedy Krieger Institute, USA; <sup>4</sup>Johns Hopkins University, School of Medicine, Department of Radiology and Radiological Science, USA; <sup>5</sup>Johns Hopkins University, School of Medicine, Department of Pathology, Division of Neuropathology, USA; <sup>6</sup>Johns Hopkins University, School of Medicine, Department of Oncology, USA; <sup>7</sup>University of Colima, Facultad de Psicología, Laboratorio de Neurociencia, Mexico; <sup>8</sup>Washington University, School of Medicine in St Louis, Department of Neurosurgery, USA  
E-mail: ijusuet1@jhmi.edu

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**Introduction:** The pathogenesis and behavioral effects of normal pressure hydrocephalus (NPH) are not fully understood, and the temporal relationship between radiological changes and neurological deterioration is unknown.

**Methods:** Bilateral subarachnoid injections of kaolin were administered in the cranial convexities of 20 adult rats. MRI was obtained using a Bruker Biospec 11.7 T MRI scanner at 14, 60, 90 and 120 days post kaolin injection. Locomotor, gait, and cognitive studies were performed independently every 2 weeks by faculty blinded to the imaging results. Tests included open field test, gait analysis, rotarod and novel object recognition. Logistic regression analysis was performed to assess association between ventricular size and clinical deterioration and rate of ventricular size enlargement and clinical deterioration.

**Results:** Radiological ventricular size showed progressive growth over time at all times ( $p < 0.0001$ ). The fastest ventricular enlargement happened within the first two months. No changes in gait, cognition, anxiety and general locomotor activity were detected during the first two months. The first gait deterioration occurred at 69 days; anxiety at 80 days; cognitive at 81 days and locomotor after 120 days. At the end of the study 66% of rats developed gait deterioration, 66% cognitive deterioration and 83% anxiety changes. Ventricular enlargement was not associated with gait ( $p > 0.05$ ), cognitive ( $p > 0.05$ ) or anxiety ( $p > 0.05$ ) deterioration. Locomotor deterioration was associated with ventricular size ( $p = 0.014$ ), speed of ventricular enlargement ( $p = 0.015$ ) and extension of injected kaolin ( $p = 0.04$ ).

**Conclusions:** Kaolin injected in the subarachnoid space of adult rats can produce slow onset communicating hydrocephalus. Initially the ventricular enlargement seen on images is asymptomatic. Ventricular enlargement does not correlate with clinical impairment with exception of delayed locomotor impairment.

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#### O14

##### Three-hundred cases of Spiegelberg ICP monitoring for hydrocephalus and CSF disorders: the Queen Square experience

Aswin Chari<sup>1</sup>, Edward W Dyson, Andrew R Stevens, Simon D Thompson, Claudia Craven, Samir A Matloob, Huan Wee Chan, Syed N Shah, Tarek Mostafa, Neekhil A Patel, Jinendra Ekanayake, Patricia Haylock-Vize, Ahmed K Toma, Laurence D Watkins  
Victor Horsley Department of Neurosurgery, National Hospital For Neurology and Neurosurgery, UK  
E-mail: aswinchari@gmail.com  
*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:O14

**Introduction:** Although invasive intracranial pressure monitoring (ICPM) has been a mainstay in the management of traumatic brain injury for a number of years, its use in an elective or emergency setting to guide management of patients with hydrocephalus and other CSF disorders is a relatively new concept. This single centre experience examines the safety profile and utility of ICPM in this patient population.

**Methods:** We retrospectively reviewed all cases of monitoring over a 10 year period at the National Hospital for Neurology and Neurosurgery, London, UK. 338 cases were identified. Case records were reviewed for diagnosis, indication of ICPM, duration, complications and outcome. All operations utilised Spiegelberg ICP monitors, inserted in a protocolised fashion under sedation.

**Results:** ICPM was undertaken for a number of different conditions including undiagnosed headache (20.4%), IIH (28.7%), NPH (5.3%), high-pressure

hydrocephalus (eg congenital/post-traumatic/post-SAH) (17.2%) and Chiari malformations/syringomyelia (13.6%). Indications for ICPM included headache (74.0%), visual disturbance (6.2%), gait disturbance (6.2%) and cognitive disturbance (5.0%). Mean monitoring time was 37.3 hrs (range 12-154 hrs). Monitoring was conducted in the presence of a CSF shunt (50.6%), venous stent (3.7%) and previous cranial decompression (6.5%). Dynamic monitoring (eg with different shunt settings or pre/post venous stent insertion) was undertaken in 12.4%. Outcomes from ICPM included insertion of new CSF shunt (21.0%), revision of CSF shunt (13.0%), insertion of venous stent (6.5%), insertion of and lumbar drains for infusion studies (3.6%); importantly, non-operative treatment was pursued in a number of cases including shunt valve adjustment (7.7%) and conservative management (29.9%). Complications included superficial infection (4 patients, 1.2%), symptomatic intracerebral haematoma (1 patient, 0.3%) and misplacement (3 patients, 0.9%); importantly, there were no cases of deep intracranial infection and the only case of seizures was in the patient with the intracerebral haematoma.

**Conclusion:** This is the largest known series of ICPM for CSF disorders. It shows that ICP monitoring is a safe procedure and may be undertaken as part of routine protocol in the management of complex hydrocephalus patients. The number of cases that were subsequently managed conservatively or with a simple valve adjustment (37.6%) indicates the utility in terms of reducing operative interventions. Further evaluation of positive and negative predictive values based on the results of ICP monitoring and health-economic analyses will push the case for routine ICP monitoring prior to definitive management of all hydrocephalus patients.

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#### O15

##### Natural history of Endoscopic Third Ventriculostomy followed with high resolution MRI

Miguel Trelles<sup>1,2\*</sup>, Ignacio Jusue-Torres<sup>1</sup>, Charles Mitchell<sup>1</sup>, Solomon David<sup>1</sup>, Eric W Sankey<sup>1</sup>, Rigamonti Daniele<sup>1</sup>, Ari Blitz<sup>1</sup>  
<sup>1</sup>Clinica Delgado, Lima, Peru; <sup>2</sup>Johns Hopkins Hospital, Maryland, USA  
E-mail: m\_trelles@hotmail.com  
*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:O15

**Introduction:** Endoscopic third ventriculostomy (ETV) is a common procedure utilized to treat non-communicating hydrocephalus. The purpose of this study is to evaluate the morphologic change seen in ETV in adult hydrocephalus defects over time in with constructive interference in steady state (CISS) high resolution MRI.

**Methods:** A retrospective review of all post-surgical ETV high resolution MRIs from July 2009 to March 2015 with sagittal CISS images through the midline was performed. Patients with prior surgeries including ventriculostomy tubes were excluded. The ETV defect size was measured in AP and TV dimension by two experienced users. The intraclass correlation coefficient was calculated.

**Results:** 34 patients with 98 studies were included. Patients had up to 4 follow up studies up to 4 years after ETV surgery. The average defect size on the immediate post-surgical study was 2.2 x 2.4mm (ellipsoid area of 4.6mm<sup>2</sup>). Two patients had their ETVs close during the studied

time (2/34, 6%). All other patients showed an increase in size of the ETV defect during the studied time. The average increase was of 0.02 mm<sup>2</sup>/day or 7.3 mm<sup>2</sup>/year with greater increase in the first post surgical year. Intra-class correlation coefficient between measurement was 0.83 and 0.88 for the AP and TV measurement respectively. Clinical data showed larger defects on last follow-up and higher speed of enlargement in older individuals.

**Conclusion:** High resolution MRI with sagittal CISS images is useful in the post-operative evaluation of ETVs. A small percentage closed in the first year of follow up with increase in size of the ETV defect on all other patients suggesting the possibility of a size threshold for continued patency in adults.

## O16

### Influence of vascular risk factors and vascular disease on long-term outcome in idiopathic Normal Pressure Hydrocephalus; a Quality Registry based study

Kerstin Andrén<sup>1\*</sup>, Carsten Wikkelso<sup>1</sup>, Nina Sundström<sup>2</sup>, Katarina Laurell<sup>2</sup>, Babar Kahlon<sup>3</sup>, Per Hellström<sup>1</sup>, Mats Tullberg<sup>1</sup>

<sup>1</sup>Institute of Neuroscience and Physiology, The Sahlgrenska Academy, University of Gothenburg, Sweden; <sup>2</sup>Department of Pharmacology and Clinical Neuroscience, Umeå University, Sweden; <sup>3</sup>Department of Neurosurgery, University Hospital, Lund, Sweden

E-mail: kerstin.andren@neuro.gu.se

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**Introduction:** Studies support a higher proportion of vascular risk factors in iNPH patients than in the general population. Less favorable outcome for patients with, than without, cerebrovascular comorbidity and vascular risk factors has been described, though in smaller studies. We investigate whether this can be confirmed in a large national Quality Registry based study.

**Methods:** Pre- and postoperative data were extracted from the Swedish Hydrocephalus Quality Registry (SHQR) on all iNPH patients (n=981) operated 2004-2011 including ordinal scales for gait, balance and continence, Mini Mental State Examination and Modified Rankin Scale (mRS), incidence of hypertension, diabetes, heart disease or stroke. In addition, data were collected from follow-up letters at 2-10 years after surgery: a self-evaluation form describing patients' present function and subjective comparison to their pre-operative condition.

A control population is currently being selected by the Bureau Statistics Sweden and data from the Swedish Registry of Cause of Death will be obtained for patients and controls; an ongoing expansion of the project.

**Results:** At time of inclusion in the registry n=434 (50%) had hypertension, n=186 (21%) had diabetes, n=119 (14%) were stroke-sufferers and n=229 (26%) had heart disease. The magnitude of change in the different outcome measures 3 months after surgery was not influenced by any of the risk factors investigated.

After 2 and 5 years, the proportion of patients who survived was smaller for patients with heart disease than without heart disease, but similar for the other three vascular factors.

In total, n=623 (64%) of patients returned 925 follow-up letter responses 3.5 ±1.4 (mean, SD) years after surgery; 2 and 5 year data are reported here.

Two and 5 years after surgery, 61.3% and 64.7% respectively, reported themselves still improved. Vascular factors did not influence the subjective reports of improvement.

Univariate analysis 2 years postoperatively for each of the four reported vascular factors showed no increased risk for poor outcome, defined as mRS 3-5 or 6 (deceased). At 5 years postoperatively OR for poor outcome with heart disease at baseline was 3.04 (1.52-6.05 95%CI), p=0.002; stroke OR 2.93 (1.11-7.70 95%CI), p=0.029; diabetes OR 2.43 (1.15-5.17 95%CI), p=0.021; Hypertension n.s.

**Conclusion:** Preliminary results from this Quality Registry based study with 981 iNPH patients suggest that co-occurrence of vascular factors do not increase the risk for poor outcome within 2 years from shunt surgery, but at 5 years postoperatively there is an increased risk. For surviving patients, the vascular risk factors have no influence on the proportion reporting themselves still improved 2 and 5 years after surgery.

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## O17

### Towards a better understanding of the cellular basis for cerebrospinal fluid shunt obstruction: report on construction of a bank of explanted hydrocephalus devices

Brian W Hanak<sup>1\*</sup>, Emily F Ross<sup>1</sup>, Carolyn A Harris<sup>2</sup>, Samuel R Browd<sup>1</sup>, William Shain<sup>1</sup>

<sup>1</sup>University of Washington, Seattle, WA, USA; <sup>2</sup>Wayne State University, Detroit, MI, USA

E-mail: hanakb@uw.edu

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**Introduction:** Shunt obstruction with cells/tissue is the most common cause of shunt failure; with ventricular catheter obstruction, alone, accounting for >50% of pediatric failures. We sought to systematically collect explanted ventricular catheters from Seattle Children's Hospital with a focus on elucidating cellular mechanisms underlying obstruction.

**Methods:** In the operating room explanted hardware was placed in 4% paraformaldehyde. Weekly, samples were transferred to buffer solution and stored at 4°C. After obtaining consent/assent, catheters were labeled using cell-specific markers for astrocytes (monoclonal rat anti-gial fibrillary acidic protein), microglia (monoclonal rabbit anti-Iba1), and choroid plexus (polyclonal chicken anti-transferrin) for 24 hrs. These targets were visualized using goat anti-rat Alexa 488, goat anti-rabbit Alexa 594, and goat anti-chicken Alexa 647 conjugated secondary antibodies, which were applied for 24 hrs in conjunction with a nuclear stain (Hoechst). Catheters were mounted in custom polycarbonate imaging chambers. Three-dimensional, multispectral spinning disk confocal microscopy was utilized to image catheters (Olympus, IX81 inverted microscope, motorized stage, charged-coupled camera).

**Results:** Intraoperatively confirmed ventricular catheter obstruction was the leading cause of shunt failure, noted in 53.6% of cases. Shunt hardware was explanted in 321 surgeries during the study period (4/1/13 – 11/30/14) and we received hardware in 34.0% of cases. Our consent rate for explanted ventricular catheters was 58.2%. Bugbee wire monopolar electrocautery was used on 26.1% of explanted catheters. Over 30 ventricular catheters have been imaged to date, resulting in the following observations: 1) Astrocytes and microglia are the dominant cell types bound directly to catheter surfaces; 2) Cellular binding to catheters is ubiquitous even if no grossly visible tissue is apparent; 3) Commercially available catheters contain rough, irregular surfaces, particularly at CSF intake holes, and there appears to be preferential cell binding to these rough surfaces; 4) Immunohistochemistry techniques are of limited utility when a catheter has been exposed to Bugbee wire electrocautery.

**Conclusions:** Ventricular catheter occlusion remains a significant source of shunt morbidity in the pediatric population and, given their ability to intimately associate with catheter surfaces, astrocytes and microglia appear to be critical to this pathophysiology. Reduced shunt failure rates may be possible through improved ventricular catheter design. Work is ongoing to fabricate catheters with smooth CSF intake portals and altered surface chemistry, with the goal of making catheters a less favorable substrate for cell attachment.

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## O18

### Risk factors for post-hemorrhagic hydrocephalus among infants with intraventricular hemorrhage

Hannah M Tully<sup>1,2,3\*</sup>, Christopher M Traudt<sup>2,3</sup>, Tessa Rue<sup>3</sup>, Assaf P Oron<sup>1</sup>, Tamara D Simon<sup>1,2</sup>, Walter A Kukulj<sup>3</sup>, Dan Doherty<sup>1,2,3</sup>  
<sup>1</sup>Seattle Children's Research Institute, USA; <sup>2</sup>Seattle Children's Hospital, USA; <sup>3</sup>University of Washington, USA  
E-mail: hmtully@uw.edu

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**Introduction:** Post-hemorrhagic hydrocephalus (PHH) is a common complication of intraventricular hemorrhage (IVH) of prematurity, but the risk factors that predispose infants with IVH to PHH have not been fully elucidated.

**Methods:** Retrospective cohort study of infants diagnosed with IVH between 2004 and 2014, with and without PHH, from the Pediatric Hospital Information System, which contains data from 44 American children's hospitals. Poisson regression was used to calculate adjusted risk ratios (RRs) and 95% confidence intervals (CIs) for multiple potential risk factors, stratified by IVH grade (I/II, III/IV).

**Results:** Among 19,077 infants with IVH who lived at least 60 days, 2,422 (12.7%) developed PHH, including 233 (1.9%) of 12,078 infants with Grade I/II IVH and 1,917 (37.1%) of 5,165 infants with Grade III/IV IVH. Among the infants with Grade III/IV IVH, Hispanic and Asian ethnicity were associated with a reduced risk of PHH compared to whites (RR: 0.84, 95%CI: 0.75, 0.93; RR: 0.63, 95%CI: 0.43, 0.92, respectively). Meningitis was associated with an increased risk of PHH (RR: 2.42, 95%CI: 2.25, 2.61). Patent ductus arteriosus was associated with a reduced risk, (RR: 0.80, 95%CI: 0.75, 0.86), as was use of the NSAID indomethacin, used to treat PDA (RR: 0.67, 95%CI: 0.60, 0.76). Atropine and dexamethasone were associated with increased risk (RR: 1.48, 95%CI: 1.38, 1.59; RR: 1.14, 95%CI: 1.06, 1.23). Pressors, nitric oxide and steroids (other than dexamethasone) were all associated with reduced risk (RR: 0.64, 95%CI: 0.60, 0.69; RR: 0.69, 95%CI: 0.55, 0.86; RR: 0.71, 95%CI: 0.64, 0.79).

**Conclusions:** Several innate, acquired and potentially modifiable exposures appear to influence the development of PHH among infants with IVH. The reduced risk associated with certain classes of medication such as pressors, NSAIDs and steroids warrants further investigation.

## O19

### Novel cerebrospinal fluid inflammatory biomarkers in neonatal post-hemorrhagic hydrocephalus

Gakwaya Habiyaremye<sup>1</sup>, Diego M Morales<sup>1</sup>, Clint D Morgan<sup>2</sup>, James P McAllister<sup>1</sup>, David D Limbrick<sup>1</sup>

<sup>1</sup>Department of Neurological Surgery, Division of Pediatric Neurosurgery, Washington University, St. Louis, MO, USA; <sup>2</sup>Vanderbilt University School of Medicine, Nashville, TN, USA

E-mail: habiyaremyeg@wudosis.wustl.edu

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**Introduction:** Although inflammation is believed to play a major role in the pathogenesis of post-hemorrhagic hydrocephalus (PHH), a comprehensive characterization of cerebrospinal fluid (CSF) inflammatory biomarkers in PHH has not been performed. Therefore, the aim of this study is to measure concentrations of chemokine and cytokine biomarkers that have yet to be studied in neonatal PHH. These biomarkers include CCL-3, CXCL-12, CX3CL-1, IL-10 and P-selectin.

**Methods:** ELISA was used to measure CSF inflammatory biomarker concentrations in 10-15 patients per study group. Study groups included PHH-LP (lumbar puncture) and age-matched pre-term controls (PT). PHH-LP and PT samples were collected perinatally during spinal tap.

**Results:** CCL-3, IL-10 and P-selectin were significantly increased in PHH-LP with corresponding p values of 0.0001, 0.0001, and 0.0009. No difference was found in CXCL-12 and CX3CL-1.

**Conclusions:** Our findings suggest that CCL-3, IL-10 and P-selectin contribute to the inflammatory process in neonatal PHH. CXCL-12 and CX3CL-1 findings indicate that these biomarkers may not be involved in neonatal PHH inflammatory processes. Interestingly, CCL-3 appears to be an important driver of acute inflammation; it potently attracts neutrophils and other polymorphonuclear-lymphocytes causing secondary injury to brain tissue by generating ROS and secreting pro-inflammatory proteases. These findings suggest that a chronic neuroinflammatory process accompanies PHH and the differential changes in biomarkers help inform future studies of pharmacological modulation.

## O20

### Cerebrospinal fluid biomarkers of malfunctioning ventriculoperitoneal shunts: a pilot study

Clinton David Morgan<sup>1\*</sup>, Diego M Morales<sup>2</sup>, Gakwaya Habiyaremye<sup>2</sup>, James P McAllister<sup>2</sup>, David D Limbrick<sup>2</sup>

<sup>1</sup>Department of Neurological Surgery, Vanderbilt University School of Medicine, Nashville, TN, USA; <sup>2</sup>Department of Neurological Surgery, Division of Pediatric Neurosurgery, Washington University, St. Louis, MO, USA

E-mail: clint.d.morgan@gmail.com

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**Introduction:** Ventriculoperitoneal shunts (VPS) are a critical feature of management of pediatric hydrocephalus. Unfortunately, shunt failure is often unrecognized before significant symptoms and focal signs present, requiring costly emergency room visits and neuroimaging. Ventricular CSF biomarkers of neuropathology and neurodevelopment are emerging as critical predictors of real-time physiology in pediatric hydrocephalus. Moreover, in the future, biomarkers of neuropathology could be pre-operatively analyzed from shunts in question, reducing unnecessary surgical exploration. In this pilot study, CSF samples taken during surgical exploration were compared, hypothesizing that two critical CSF proteins, amyloid precursor protein (APP) and neural cell adhesion molecule (NCAM-1), known to be elevated in untreated hydrocephalus, may discriminate between functioning and malfunctioning shunts.

**Methods:** Approval from the Washington University Human Research Protection Office was acquired, and a pediatric CSF repository was established. All patients prospectively enrolled were between 0-4 years of age and were undergoing surgical exploration of proximal, valve, and distal components of VPS for suspected CSF diversion failure. CSF was acquired in the operating room under sterile conditions, transported on ice, centrifuged, and supernatant was stored at -80°C until experimental analysis. Enzyme-linked immunosorbent assay (ELISA) was used to examine CSF concentration of APP and NCAM-1. Total protein was assessed using a standard Pierce Bicinchoninic Acid (BCA) protein assay kit. A microplate reader was used to assess biomarker concentration (ng/mL). Mann-Whitney U analysis was used for comparison of these non-parametric data, with statistical significance threshold set a priori at p<0.05.

**Results:** Twenty eight patients were found to have malfunctioned VPS, while 5 were found to have functioning VPS. There were no significant differences in age at the time of ventricle CSF sample (p=0.07), levels of total CSF protein (p=0.335), total APP (p=0.516), or total NCAM (p=0.816) concentrations. However, due to the fact that there is significant inter-individual variation in CSF total protein levels, we compared normalized APP (nAPP) and normalized NCAM-1 (nNCAM) between the two groups.

Patients found to have nonfunctioning shunts had a significantly elevated nAPP (p=0.044) and tended to have elevated nNCAM (p=0.061) when compared to patients with functioning shunts.

**Conclusions:** nAPP and nNCAM concentrations in ventricular CSF may be elevated in malfunctioning VPS, when compared to similarly aged patients with functioning shunts. While this is a small pilot study, active enrollment continues of new patients into this study given its potential implications.



## O21

### Differences in intracranial pressure seen in children and adults could be caused by age differences

Sarah Skovlunde Hornshøj Pedersen<sup>\*</sup>, Alexander Lilja Jørgensen, Morten Andresen, Trine Hjorslev Andreasen, Marianne Juhler  
CSF Copenhagen Studygroup, Denmark  
E-mail: sarahshpedersen@gmail.com  
*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:O21

**Introduction:** In neurosurgery, one aim of treatment is normalization of intracranial pressure (ICP). Although a range from 7 to 15 mmHg is widely accepted in neurosurgical clinical practice, true reference values are uncertain. No studies compare ICP measurements in children to measurements in adults, and it seems silently assumed that reference values are the same. The same reference range is therefore, regardless of the physiological differences, used for both children and adults.

This study has two aims:

- To clarify if day and night ICP differs between children and adults.
- To examine if age affects ICP.

**Methods:** We analysed data from all non-shunted patients undergoing invasive elective diagnostic ICP monitoring from February 2008 to November 2014.

Data from 24 hours of ICP monitoring were separated into day and night sequences. The minimum, maximum, and mean values were determined for both sequences. The first hour of monitoring following probe implantation was discarded to allow for initial stabilization following surgery. To ensure consistency, the same person analysed all ICP monitoring sessions.

**Results:** We included 130 patients (58 children, mean age=9.0 years, range 1-17. 72 adults, mean age=50.1 years, range 18-85).

We found that nocturnal ICP increased in 95% of the patients. Looking at  $\Delta$ ICP (for day and night pressure) the intrapersonal difference was nearly identical in children (mean 6.6 mmHg) and adults (6.3 mmHg)  $p=0.798$ . However, there were noteworthy differences between children and adults;

- Children had both higher mean ICPday (6.3 vs. 2.5 mmHg,  $p<0.001$ ) and mean ICPnight (12.6 vs 8.9 mmHg,  $p<0.001$ ) than adults.
- In adults we found that both ICPday and ICPnight decreased with age (decrement of 0.1 mmHg per year).
- In children only ICPday decreased with age (decrement of 0.45 mmHg per year).

**Conclusion:** We found that both children ( $p<0.001$ ) and adults ( $p<0.001$ ) displayed higher ICP values at night, and the difference between night and day was comparable between the groups.

Measured ICP values were higher in children than in adults both day and night.

We furthermore found that ICP could be described as a linearly decreasing function of age. This could indicate that the ICP reference values for children should be different than those for adults.

The results are important for clinical management of paediatric ICP and contribute to the understanding of the basic physiology of the brain.

## O22

### Shunt revision requirements after posthemorrhagic hydrocephalus of prematurity: insight into the time course of shunt dependency

Edward Ahn<sup>\*</sup>, Joanna Wang, Eric Jackson, George Jallo  
Johns Hopkins University School of Medicine, USA  
E-mail: eahn4@jhmi.edu  
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**Introduction:** Intraventricular hemorrhage (IVH) is a common affliction of preterm infants, and often results in posthemorrhagic hydrocephalus (PHH). These patients typically eventually require permanent CSF diversion and are presumed to be indefinitely shunt-dependent. To date, however, there has been no study of long-term shunt revision requirements in patients with PHH.

**Methods:** We analyzed retrospectively collected data for 89 preterm patients diagnosed with Grade III and IV IVH and PHH at our institution from 1998 to 2011.

**Results:** 69 out of 89 patients (77.5%) underwent VP shunt placement, and 33 (47.8%) required at least one shunt revision and 18 (26.1%)

required multiple revisions. The mean  $\pm$  standard deviation follow-up time for shunted patients was  $5.0 \pm 3.3$  years. The majority of early failures are due to proximal catheter malfunction, while later failures were mostly due to distal catheter problems. There was a significant difference in the number of patients requiring revisions in the first three years following initial VP shunt insertion compared after three years, with 28 revisions versus 10 ( $p<0.004$ ). In the 10 patients who underwent shunt revisions after three years, evidence of obstructive hydrocephalus was found on imaging either in the form of an isolated fourth ventricular cyst or aqueductal stenosis.

**Conclusions:** Our results suggest that in a distinct subset of patients with PHH, obstructive hydrocephalus may develop, resulting in long-term dependence on CSF diversion. Further study on the factors associated with long-term shunt dependence and revision requirements within the PHH group is warranted.

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## O23

### The role of perfusion and diffusion MRI in the management of patients affected by probable iNPH: A cohort-prospective preliminary study

Francesco Tuniz<sup>\*</sup>, Maria Caterina Vescovi, Maria Cristina DeColle, Daniele Bagatto, Marta Maieron, Miran Skrap  
Azienda Ospedaliero Universitaria SM Misericordia, Italy  
E-mail: tunizfrancesco@gmail.com  
*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:O23

**Introduction:** Two invasive tests are mainly used to select patients affected by NPH for surgery: measuring resistance to CSF outflow and Tap Test. Cerebral blood flow (CBF) have been demonstrated to be reduced in iNPH patients, mainly in basal ganglia (BG) and periventricular white matter (PVWM) regions. Perfusion MRI might be of value as a diagnostic and predictive tool. The rule of diffusion MRI in determining brain damage in PVWM and BG areas have been investigated. The aim of this study is to identify relationship between cerebral perfusion and microstructural damage of brain tissue measured by perfusion and diffusion MRI in PVWM and BG areas before and after tap-test and after surgery in patients who underwent VP shunt.

**Methods:** 23 patients were included in this study. MRI related rCBF and apparent diffusion coefficient (ADC) were calculated in all the cases. Regions of interest were located in PVWM and BG areas. Each patient underwent lumbar infusion test and tap test. After these tests were performed, patients have been clinically evaluated and another MRI was performed with the same protocol. Patients have been then divided into two groups: the first cohort that improved after Tap test, and the second

one that did not. Only the first group underwent surgery and were clinically and radiological assessed again a month after VP shunt implantation. A descriptive statistical study was performed using non parametrical tests.

**Results:** All the 13 patients surgically treated presented a clinical improvement after surgery; an significant increase in rCBF in both periventricular and basal ganglia regions after tap-test and surgery; a decrease in ADC values in periventricular region and an increase in ADC values in basal ganglia regions. The 10 negative patients shown a reduction in rCBF in both PVWM and BG after tap-test; a decrease in ADC values in PVWM and an increasing in ADC values in BG region.

**Conclusions:** Since trend of rCBF acquired by perfusion MRI agreed with invasive tests results it could be considered a predictive and effective method in the management of patients with probable iNPH. Authors hypothesized decrease in ADC value in PVWM region as a reduction of transependimal edema; and increase in ADC value in basal ganglia area as a reduction in chronic cytotoxic edema due to chronic blood flow impairment.

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#### O24

##### Game changing technology addresses unmet need in occlusion based shunt failures by providing a non-invasive solution to re-establish flow in occluded Ventricular Catheters

Andrew East<sup>1\*</sup>, Tomer Anor<sup>2</sup>, Deep Singh<sup>1</sup>, Morgan Brophy<sup>1</sup>, Greg Eberl<sup>1</sup>, PJ Anand<sup>1</sup>, JR Madsen<sup>2</sup>

<sup>1</sup>Alcyone Lifesciences, Inc., USA; <sup>2</sup>Boston Children's Hospital, USA

E-mail: aeast@alcyonels.com

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**Introduction:** Ventricular catheter (VC) occlusion due to choroid plexus is the predominant cause of shunt malfunction whose prevention remains a major unsolved problem, despite best efforts of clinicians and device designers. Shunt malfunction usually demands can be life threatening, and frequently triggers urgent nocturnal surgical intervention to revise the shunt system, costing on average ~\$34K per surgery. The total cost of shunt surgeries in the U.S. exceeds \$2 billion per year.

Clinical experience suggests that some of the occluded VCs can be unblocked by carefully "flushing" them with saline during surgery, restoring cerebrospinal fluid (CSF) flow, so potentially a pulse of retrograde flow could dislodge choroid plexus. We therefore sought to design a retrograde flushing device, used non-invasively, hoping to avoid a need for emergency surgery.

**Methods:** We therefore measured the pressure and volume ranges of the injected fluid used for flushing blocked VCs as deemed safe by expert neurosurgeons in the operating room, as approved by our IRB. Based on the surgical pressure volume impulse characteristics, an implantable device compatible with existing shunt systems was designed to simulate the surgical flushing technique. In addition to the implantable retrograde shunt flusher, a modification of the VC was designed to generate an alternative CSF flow pathway when the obstruction does not yield. Device prototypes were manufactured and extensive testing was conducted to validate design requirements.

**Results:** According to measurements taken during the study, the surgeons were typically applying up to 50 PSI of pressure within the occluded VC while injecting 0.1-0.5 cc of saline with a syringe in short

"pumps" attempting to unblock a VC. In some cases, the flushing maneuver was successful in increasing flow through the VC.

Through bench testing of the Alcyone prototype flushing technology, it has been demonstrated that a retrograde pulse of fluid can be generated, non-invasively by external manipulation, similar to the pressure and volume measurements taken in the OR.

**Conclusions:** Alcyone shunt technology provides a non-invasive solution to re-establish flow in an occluded VCs and may extend the life of the shunt, prevent revision surgeries and avoid life-threatening emergencies caused due to blocked/non-flowing shunt complications.

#### O25

##### A new electronic valve for the treatment of NPH

Christoph Miethke\*, Joerg Binkele, Thoralf Knitter

Christoph Miethke GmbH & Co KG, Germany

E-mail: ceo@miethke.com

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The first shunts being successfully used for the treatment of hydrocephalus were designed to lower an overpressure within the ventricles of the brain. Later the same technology was used for the treatment of normal pressure hydrocephalus, although the background of this disease can not be compared with obstructive hydrocephalus. Since then no specific device has been developed focussing on the treatment of NPH. However, the recent knowledge of NPH and the risks behind the shunting of NPH offer interesting options.

For the diagnosis of NPH an often used method is the spinal tap test. The withdrawal of up to 50 cc of spinal fluid sometime leads to impressive clinical improvement. To address this fact a new device has been developed which can be programmed to open depending on time and body position. Consequently in contrast to valves for the treatment of obstructive hydrocephalus this device does not open depending on increased baseline ICP or ICP peaks. The device can be programmed to open for two minutes intervals over 24 hours. The valve can be programmed to remain closed, to open for two minutes within 24 hours, to open the whole 24 hours or any time between two minutes and 24 hours. In addition it can be programmed whether or not the opening should be manipulated by the body position of the patient in particular to allow an only reduced flow in the standing position.

The new electronic device is the first implant developed only for NPH addressing specific aspects of this disease. The valve has been investigated in vitro simulating the condition within a patient. It has not been implanted yet, because of regulatory issues. Whether or not the device improved the clinical outcome in patients with NPH, whether or not it can lower risks for these patients and introduce new treatment options can not be answered without clinical experience. However, it promises to be a tool for scientific research, which might help to improve the understanding of NPH.

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#### O26

##### Adult onset aqueductal stenosis may become symptomatic due to deep white matter ischemia

William Guerin Bradley\*, Mohammed Abdihalim, Abdulrachman Almutairi UCSD, USA

E-mail: wgbradley@ucsd.edu

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**Introduction:** The term "Aqueductal stenosis" generally implies a congenital etiology which may or may not be compatible with life. Those that survive probably have an aqueductal membrane with a pinhole, allowing at least some CSF through. These patients may require an alternate CSF drainage pathway via the extracellular space (ECS) of the brain as occurs in children with tectal gliomas. It is likely that there is a "second hit" in addition to this congenital condition that leads to symptom onset in late adulthood. We hypothesize that the onset of deep white matter ischemia in late adulthood increases resistance to CSF flow through

the extracellular space of the brain, contributing to the onset of symptoms of aqueductal stenosis in late adulthood.

**Methods:** Retrospective review of our database searching for the keywords of "aqueductal stenosis" from August 2009-April 2015, yielded 15 cases of adult onset aqueductal stenosis confirmed on a midsagittal FIESTA or CISS image. The apparent diffusion coefficient (ADC) in four regions in the centrum semiovale were measured as a surrogate of the amount of water in the ECS in patients with aqueductal stenosis and in controls with the same amount of deep white matter ischemia (DWMI).

**Results:** ADC measurements performed in the centrum semiovale are significantly higher in patients with aqueductal stenosis than in controls ( $P < .01$ ), controlling for the same degree of DWMI. This indicates that there is increased fluid in the ECS of the brain of the aqueductal stenosis cases, supporting the hypothesis that the parallel pathway for CSF egress is via the ECS.

**Conclusion:** Increasing resistance to CSF outflow through the ECS of the brain due to deep white matter ischemia in late adulthood may contribute to the development of symptoms in adult onset aqueductal stenosis.

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#### O27

##### Physiological variability in CSF motion using magnetic resonance time spatial labeling inversion pulse (Time-SLIP) - real time imaging

Shinya Yamada

Toshiba Rinkan Hospital, Japan

E-mail: shinyakoro@gmail.com

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**Introduction:** The ideal tracer for studying CSF dynamics is CSF itself. In time spatial labeling inversion pulse (Time-SLIP), MR radiofrequency pulses convert specific volumes of CSF into an endogenous tracer. CSF dynamics can then be observed under physiological and pathophysiological conditions. A gate-free and fast image acquisition technique like Time-SLIP is necessary to visualize natural CSF motion, whose behavior varies with cardiac pulsation and respiration.

**Aim:** To study physiological variability in CSF motion using the MRI Time-SLIP method.

**Methods:** A real-time Time-SLIP balanced steady state free precession (bSSFP) sequence was used on 1.5T and 3T MRI scanners. Acquisition time for each image was approximately 130msec. Serial images were obtained one to five seconds after the labeling pulse. Pulsatile CSF motions over four to five cardiac strokes were analyzed.

**Result:** Considerable pulsatile CSF motion variability was observed in normal physiological brains as well as pathophysiological (hydrocephalus) brains.

**Conclusion:** Real-time MR imaging is necessary to investigate natural pulsatile CSF motion. Averaging over multiple pulsatile CSF motions potentially wipes out natural physiological variability in CSF motion.

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#### O28

##### Panventriculomegaly with a wide foramen of Magendie and large cisterna magna: clinical, radiological, and genetic analysis

Hiroshi Kageyama<sup>1,2,3\*</sup>, Ikuko Ogino<sup>1</sup>, Kazuaki Shimoji<sup>1</sup>, Madoka Nakajima<sup>1</sup>, Ryoko Fukai<sup>3</sup>, Noriko Miyake<sup>3</sup>, Kenichi Nishiyama<sup>4</sup>, Naomichi Matsumoto<sup>3</sup>, Hajime Arai<sup>1</sup>, Masakazu Miyajima<sup>1</sup>

<sup>1</sup>Juntendo University, Japan; <sup>2</sup>Kuki General Hospital, Japan; <sup>3</sup>Yokohama City University, Japan; <sup>4</sup>University of Niigata, Japan

E-mail: kageyamahiroshi29@gmail.com

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**Introduction:** The purpose of this study is to provide the first clinical, radiological, and genetic analysis of panventriculomegaly (PaVM) defined by a wide foramen of Magendie and large cisterna magna.

**Methods:** Clinical and radiological data from 28 PaVM patients (including 10 patients in 5 families) were retrospectively analyzed. Five children were included. Tetra-ventricular dilatation, aqueduct opening with flow void on T2 weighted images, and a wide foramen of Magendie and large cisterna magna were essential magnetic resonance imaging findings for PaVM diagnosis. Three-dimensional fast asymmetric spin echo sequences were used for visualization of membranes in basal cisterns. Time-spatial labeling inversion pulse examination was performed to analyze cerebrospinal fluid (CSF) movement. Gene mutations were analyzed using high-resolution microarray and validated by quantitative PCR with breakpoint sequencing.

**Results:** In adult patients, the age of onset was  $56.0 \pm 16.7$  years. It was lower than that of idiopathic normal pressure hydrocephalus (iNPH). Adult patients showed iNPH like symptoms, as gait disturbance, urinary dysfunction, and cognitive dysfunction. Five infantile patients exhibited macrocranium. Patients were divided into two subcategories, with or without downward bulging third ventricular floors and membranous structures in the prepontine cistern. CSF movement of patients with bulging floors, who had thick membranes in the prepontine cistern, was restricted in prepontine cisterns. Patients with bulging floors were successfully treated with endoscopic third ventriculostomy. Genetic analysis revealed a deletion in DNAH14 that encodes a dynein heavy chain protein associated with motile cilia function, and which co-segregated with patients in a family without a downward bulging third ventricular floor.

**Conclusion:** Panventriculomegaly with a wide foramen of Magendie and large cisterna magna may belong to a subtype of congenital hydrocephalus with familial accumulation, younger onset, and symptoms of iNPH. In addition, a PaVM family has a gene mutation associated with dysfunction of motile cilia.

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#### O29

##### Intracranial pressure guided management of patients with Chiari malformations presenting with headache: a paradigm shift?

Edward W Dyson<sup>\*</sup>, Aswin Chari, Andrew R Stevens, Miron D Thompson, Claudia Craven, Patricia Haylock-Vize, Samir A Matloob, Syed N Shah, Huan Wee Chan, Neekhil A Patel, Tarek Mostafa, Jinendra Ekanayake, Ahmed K Toma, Lewis W Thorne, Laurence D Watkins

Victor Horsley Department of Neurosurgery, National Hospital for Neurology & Neurosurgery, Queen Square, London, UK

E-mail: ewdyson@gmail.com

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**Introduction:** Chiari malformation (CM) describes cerebellar tonsillar descent below the level of the foramen magnum. It is commonly associated with syringomyelia and often presents with headache (1). The conventional surgical treatment for symptomatic patients is foramen magnum decompression (FMD) (2) which carries a significant burden of operative morbidity (3). Altered cerebrospinal fluid (CSF) dynamics have been demonstrated in CM patients and CSF diversion has been used as an alternative treatment modality. Patients with chronic headache and radiological evidence of CM represent a therapeutic challenge. In our unit, these are primarily investigated with intracranial pressure (ICP) monitoring aiming to detect objective evaluation of CSF dynamics prior to surgical intervention.

**Methods:** In this single centre, retrospective study, CM patients presenting with headaches were extracted from our departmental ICP monitoring database. Patients with an existing CSF diversion shunt or a previous foramen magnum decompression were excluded. ICP monitoring results were analysed with emphasis on median intracranial pressure (mICP) and

median pulse amplitude (mPA). Clinical records were reviewed for clinical presentation, surgical management and outcome.

**Results:** 16 patients with CM and ICP monitoring were identified. 7 had associated syringomyelia. The mean mICP across the group was  $2.97 \pm 3.13$  mmHg. Mean mPA was  $5.23 \pm 1.27$  mmHg (normal value  $\leq 4$  mmHg). All patients had mICP  $< 10$  mmHg. 2 patients had mICP  $< 0$  mmHg, 14 out of 16 patients had abnormal pulsatility (mPA  $> 4$  mmHg). 6 patients were treated with primary ventriculoperitoneal shunt (VPS) insertion, 3 underwent FMD, 1 was treated medically with acetazolamide and 5 were managed conservatively. There were no significant surgical complications in either the VPS or the FMD group. At 2 month follow-up, all patients in the VPS group experienced symptomatic improvement. 2 patients in the FMD group experienced symptomatic improvement and one was unchanged.

**Conclusions:** The majority of patients with symptomatic untreated Chiari malformation have increased ICP pulsatility (and by deduction, impaired compliance) but a "normal" overall mICP. Raw ICP values are not sensitive in identifying abnormalities of compliance in this patient group. A small group of patients may develop tonsillar descent due to relatively low ICP.

VPS insertion may be a safe, effective alternative to FMD for patients with symptomatic CM, even in the absence of hydrocephalus.

We propose routine intracranial pressure monitoring in CM patients with headache and, if indicated, cranial CSF diversion as first line management.

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#### O30

##### Brain tissue viscoelasticity in chronically shunted patients with headaches using Magnetic Resonance Elastography

Kristy Tan<sup>1\*</sup>, Adam L Sandler<sup>2</sup>, Avital Meiri<sup>1</sup>, Rick Abbott<sup>2</sup>, James T Goodrich<sup>2</sup>, Eric Barnhill<sup>3</sup>, Mark E Wagshul<sup>1</sup>

<sup>1</sup>Albert Einstein College of Medicine, USA; <sup>2</sup>Department of Neurological Surgery, Albert Einstein College of Medicine/Children's Hospital at Montefiore, Bronx NY, USA; <sup>3</sup>Clinical Research Imaging Centre, College of Medicine and Veterinary Medicine, University of Edinburgh, UK  
E-mail: [kristy.tan@einstein.yu.edu](mailto:kristy.tan@einstein.yu.edu)

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**Introduction:** Chronic headaches are a well-documented complaint of shunted hydrocephalic patients. However, it is also one of the signs of shunt malfunction. Cranial compliance deficiency may be a cause of chronic headaches in some chronically shunted patients with functioning shunts (often with slit or smaller than normal ventricles). This study aims to use a novel, non-invasive imaging technique, Magnetic Resonance Elastography (MRE) to investigate the role of brain viscoelasticity in pediatric hydrocephalic patients.

**Methods:** Shunt-dependent patients who developed hydrocephalus as infants were selected. Preliminary results from 12 patients (age 15-37, median age 23) who suffer from chronic headaches (excluding patients with abnormally large ventricles, defined as ventricular volume  $< 25$  cm<sup>3</sup>) are shown.

MRE was performed by inducing a mechanical wave at 30Hz, transmitted through the zygomatic arches. Wave propagation speed was used to estimate viscoelasticity (shear modulus, G\*). Images were motion and distortion corrected using MRE magnitude and field maps respectively. Image segmentation was performed on registered high-resolution images to produce CSF, white and gray matter masks using FSL. Ventricular volume was calculated from the CSF component.

**Results:** Good wave penetration was observed in MRE results allowing high quality data to be reconstructed. The viscoelasticity for gray matter was found to be positively correlated to white matter ( $R^2=0.97$ ,  $p<0.01$ ). There was a positive correlation between the viscoelasticity of gray matter and ventricular volume that was statistically significant ( $R^2=0.60$ ,  $p=0.04$ ). There was also a trend toward significance between the viscoelasticity of the white matter and ventricular volume ( $R^2=0.49$ ).

**Conclusions:** This pilot study demonstrates that MRE could be a powerful diagnostic tool to be used in pediatric hydrocephalic patients. Preliminary results show the brain to be more viscoelastic as ventricle size increases in patients indicating that compliance could be key in understanding the cause of headaches in chronically shunted patients. This study is ongoing with the aim of comparing control and patient data and correlating viscoelasticity to headache severity.

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#### O31

##### Diffusion Tensor Imaging in chronically shunted patients

Kristy Tan<sup>1\*</sup>, Adam L Sandler<sup>2</sup>, Avital Meiri<sup>1</sup>, Rick Abbott<sup>2</sup>, James T Goodrich<sup>2</sup>, Asif K Suri<sup>1</sup>, Michael L Lipton<sup>1</sup>, Mark E Wagshul<sup>1</sup>

<sup>1</sup>Albert Einstein College of Medicine, USA; <sup>2</sup>Department of Neurological Surgery, Albert Einstein College of Medicine/Children's Hospital at Montefiore, Bronx, NY, USA

E-mail: [kristy.tan@einstein.yu.edu](mailto:kristy.tan@einstein.yu.edu)

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**Introduction:** Chronically shunted patients with functioning shunts are often characterized as having slit or smaller than normal ventricles and chronic headaches. In this study, we used Diffusion Tensor Imaging (DTI) to quantitatively analyze the directionality of water diffusion in the internal capsule (IC) and the corpus callosum (CC) in these patients which have been shown to be affected in untreated hydrocephalus patients [1].

**Methods:** Shunt-dependent patients who developed hydrocephalus as infants were selected. Preliminary results from 17 patients who suffer from chronic headaches (excluding patients with abnormally large ventricles) are shown in comparison to age and gender matched controls. DTI data was acquired using a single-shot EPI sequence with TE/TR=69/10000ms, voxel size= 2mm x 2mm x 2mm, max b-factor=800, num. of directions=32. White matter ROIs were manually drawn on high-resolution T1-weighted images with the aid of fractional anisotropy (FA) maps to locate the internal capsule (IC) (right and left, anterior and posterior limbs), genu and splenium of the corpus callosum (CC) and were verified by a neuroradiologist.

**Results:** A statistically significant decrease (student t-test,  $p<0.05$ ) in FA was found in the patient group compared to the controls in the right posterior (FA=0.61 vs 0.65,  $p=0.0045$ ), left posterior (FA=0.61 vs 0.66,  $p<0.001$ ) and left anterior IC (FA=0.56 vs 0.63,  $p=0.0031$ ) as well as the splenium of the CC (FA=0.69 vs 0.80,  $p<0.001$ ). No correlations were found between ventricular volumes with the DTI parameters.

**Conclusions:** This study is the first to use DTI to study chronically shunted patients and shows evidence of white matter degradation based on decreases in FA in patients compared to controls. Previous studies have shown increased FA values in the IC and a decrease in the CC of

patients and hypothesized that it was due to an increase of mechanical compression whilst others have hypothesized that a decrease in FA indicated secondary irreversible, degenerative changes [1-3]. These studies were performed on younger patients pre-treatment who usually have enlarged ventricles and we hypothesize that this may be the source of the difference coupled with the chronic shunt dependence within our patient group.

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#### O32

##### Population based incidence and outcome of surgery for adult patients with hydrocephalus in Sweden

Nina Sundström<sup>1</sup>, Jan Malm<sup>2</sup>, Katarina Laurell<sup>2</sup>, Fredrik Lundin<sup>3</sup>, Babar Kahlon<sup>4</sup>, Kristina Cesarini<sup>5</sup>, Carsten Wikkelso<sup>6</sup>

<sup>1</sup>Department of Radiation Sciences, Biomedical Engineering, Umeå University, Umeå, Sweden; <sup>2</sup>Department of Clinical Neuroscience, Umeå University, Umeå, Sweden; <sup>3</sup>Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden; <sup>4</sup>Department of Neurosurgery, University Hospital, Lund, Sweden; <sup>5</sup>Department of Neuroscience, Neurosurgery, Uppsala University, Uppsala, Sweden; <sup>6</sup>Institution of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden

E-mail: nina.sundstrom@vll.se

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**Background:** Incidence and clinical outcome of adult hydrocephalus surgery has never been described in a large population based material. The objective of this study was to present these parameters based on data from the Swedish Hydrocephalus Quality Registry (SHQR). The registry is web-based and contains all adult hydrocephalus patients operated on in four out of five surgical units in Sweden.

**Method:** All patients registered in the SHQR during 2004-2011 were included in the study. Data on age, gender, diagnosis and type of surgery were extracted as well as three months outcome for patients with idiopathic normal pressure hydrocephalus (iNPH). Types of surgeries were shunt insertion and endoscopic third ventriculostomy (ETV).

**Results:** 2360 patients were operated on. Mean total incidence of surgery was 5.1±0.9 surgeries/100000/year; 4.7±0.9 shunt surgeries and 0.4±0.1 ETVs. For iNPH, secondary communicating hydrocephalus and obstructive hydrocephalus the incidence of surgery was 2.2±0.8, 1.9±0.3 and 0.8±0.1/100000/year respectively. During 2004-2011 the surgical incidence increased in total (p=0.044) and specifically in the age intervals 70-79 years and ≥80 years (p=0.012 and p=0.031). Improvement ≥1 step on the modified Rankin scale (mRS) was seen in 253 of 652 iNPH patients (38.8%) after surgery. Numbers needed to treat was 3.0 for improving one patient from the unfavourable (mRS 3-5) to the favourable (mRS 0-2) group. According to a modified iNPH scale 58% (range 49.3-65.1%, n=704) of the

iNPH patients improved. No significant regional differences in incidence, surgical techniques or outcome were found.

**Conclusion:** Hydrocephalus surgery increased significantly in frequency in 2004-2011 and specifically in elderly patients. The resulting incidence was however still very low. Surgical treatment for iNPH was a powerful tool for achieving functional independence, as shown by the low NNT, but the clinical outcome was not as good as recently published results. This indicates that outcome reported from clinical studies is not directly comparable to outcome based on everyday hospital assessments among unselected patients representing everyday hospital care.

#### O33

##### Acoustic schwannomas are often accompanied with disproportionately enlarged subarachnoid space hydrocephalus

Hisayuki Murai<sup>1</sup>, Toshimasa Shin, Yoshinori Higuchi, Naokatu Saeki  
Chiba University Graduate School of Medicine, Japan  
E-mail: murai@faculty.chiba-u.jp

*Fluids and Barriers of the CNS* 2015, 12(Suppl 1):O33

**Introduction:** Hydrocephalus with tight high convexity and wide Sylvian fissure is called disproportionately enlarged subarachnoid space hydrocephalus (DESH). DESH on MRI is thought to be one of the characteristic features of idiopathic normal pressure hydrocephalus (iNPH) and useful to differentiate from other ventriculomegalic status. On the other hand schwannomas are often complicated by communicating hydrocephalus, among which the expansion of the Sylvian fissure is often observed. So we examined relationship between acoustic schwannoma and communicating hydrocephalus or DESH.

**Methods:** In 178 acoustic schwannomas those are followed in our institute between April 2000 and January 2015, 19 patients, were excluded for insufficient image studies. A total of 159 cases were divided into two groups. A group without 4th ventricle deformation, its tumor size is approximately less than 3cm, comprises 122 cases. The other group with 4th ventricle deformation, its tumor size is approximately larger than 3cm, was 37 cases. In each group, the incidence of hydrocephalus or DEH was studied and was compared with the findings of iNPH epidemiological studies. Hydrocephalus was classified into DESH like and non-DESH like on CT or MRI by 2 observers. We also studied the context of a spinal fluid protein in 10 cases and spinal CSF outflow resistance in 4 cases.

**Results:** Hydrocephalus was observed in 37 (23%) out of 159 total cases. Number of DESH like hydrocephalus was 12 and non-DESH like case was 20. In 5 cases only CT scan was made and they were excluded from further analysis. In the group with 4th ventricle deformation, 18 cases (49%) presented hydrocephalus. And 5 cases (28%) showed DESH like features. On the other hand, in the group without 4th ventricle deformation the occurrence of hydrocephalus was 11% (14/122 cases). And DESH like features were observed in 50% of cases (7/14 cases). Measurement of spinal fluid proteins were conducted in 10 cases, mean value was 87 mg/dl in DESH group (6 cases) and 44 mg/dl in a non-DESH group (4 cases). Protein content was higher in DESH group, but it was not significant (p=0.075). In four cases with DESH features spinal CSF outflow resistance was measured and elevated in all cases.

**Conclusions:** Acoustic schwannomas are often complicated with hydrocephalus even in small tumor size. The incidence of hydrocephalus in group without 4th ventricle deformation is significantly higher than the general population. And DESH like findings are more common in hydrocephalus associated with small tumors. As a mechanism to exhibit DESH like features, the possibility of solute load on the CSF has been suggested, but it requires further consideration.

#### O34

##### CSF protein variations correlates with CSF oscillations in hydrocephalus patients

Olivier Balédent<sup>1,2\*</sup>, Vincent Puy<sup>1</sup>, Jadwiga Zmudka<sup>2,3</sup>, Cyrille Capel<sup>1,2</sup>, Roger Bouzerar<sup>1,2</sup>, Jérôme Ausseil<sup>1,4</sup>

<sup>1</sup>University hospital of Piarly Jules Verne, Amiens, France; <sup>2</sup>BioFlowImage, University of Piarly Jules Verne, Amiens, France; <sup>3</sup>General Hospital, Saint Quentin, France; <sup>4</sup>Inserm U1088, France  
E-mail: olivier.baledent@chu-amiens.fr

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**Introduction:** There are no previous reports comparing CSF biochemistry and its flow dynamics. As suggested by Milhorat, the complex system of CSF circulation through the brain may help to maintain a balance between the CSF flow rate and the CSF biochemical composition between different compartments. We hypothesize that this equilibrium may be disturbed in hydrocephalus patients and by using flow-MRI and CSF biological assessment, we could determine if alterations of CSF flow found in hydrocephalus patients affects their CSF biochemistry.

**Methods:** 9 hydrocephalus patients, 73 ± 8 years old, underwent a morphological MRI in which two CSF flow acquisitions were added to quantify CSF stroke volume in the aqueduct and in the spinal canal. A dynamic CSF index (Dynindex) was calculated equal to the product of the two CSF stroke volumes and to the cardiac cycle duration.

All patients had a CSF tap test insertion of a shunt. During these operations, CSF was collected from both the ventricular and spinal compartments. From these CSF samples, standard biochemical measurements were performed including chlorine, glucose and protein levels. For each CSF analysis, a biochemical ratio (Biochratio) was defined by divided the ventricular concentration by the spinal concentration.

**Results:** The ventricular and spinal CSF stroke volumes were heterogeneous among the 9 patients. In comparison with previous normal aging investigations, stroke volumes were respectively in the aqueduct and the spinal compartments: diminished (n= 1, n = 1); normal (n=3, n=4) and increased (n=5, n=4). The Dynindex varied from 0 to 100 with a mean value equal to 35. No difference between the ventricular and the spinal compartment was found for the concentrations of chlorine and glucose, and their Biochratio were respectively: 0,99±0.01 and 0,91±0.10. In contrast, the Biochratio of the protein demonstrated very different values amongst the population (from 1.21 and 5.58) and for each patient, Biochratios were strongly correlated (R=0.98, P<5.10<sup>-5</sup>) with the corresponding Dynindex.

**Conclusion:** In this small hydrocephalus population, CSF flow varied between the ventricles and the spinal compartments. Chlorine and glucose concentrations were equal in the ventricles and the spine, but protein concentration was different between the ventricles and spine and was highly correlated with the CSF flow oscillations.

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#### O35

##### The Wisconsin Hydrocephalus Survey: shunt-dependent hydrocephalus management style among members of the American Society of Pediatric Neurosurgeons

Mark Richard Kraemer<sup>1</sup>, Bermans J Iskandar  
Department of Neurological Surgery, University of Wisconsin School of Medicine and Public Health, USA  
E-mail: mrkraemer@wisc.edu  
*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:O35

**Introduction:** This survey sought to evaluate differences in the understanding and management of shunt-dependent hydrocephalus among the senior North American Pediatric Neurosurgery membership.

**Methods:** Surveys were sent to all active American Society of Pediatric Neurosurgeons (ASPN) members from September to November 2014. A total of 204 surveys were sent from which 130 responses were recorded, representing 64% of active ASPN membership. Respondents were asked 13 multiple choice and free response questions focusing on four problems encountered in shunted hydrocephalus management: Shunt malfunction, cerebrospinal fluid (CSF) overdrainage, chronic headaches and slit ventricle

syndrome (SVS). Qualtrics® online survey software was used to distribute and collect response data.

**Results:** ASPN surgeons prefer three varieties of shunt valves: 41% differential pressure, 29% differential with anti-siphon device (ASD), and 27% programmable. Respondents agree shunt obstruction occurs most often at the ventricular catheter due to either in-growth of the choroid plexus (67%), CSF debris (18%), ventricular collapse (8%), or other reasons (9%). Underlying causes of obstruction were attributed to small ventricular size, catheter position, choroid plexus migration, build-up of cellular debris, inflammatory processes, or CSF overdrainage. The majority of respondents (>85%) consider chronic overdrainage a rare complication. These cases are most often managed with ASDs or programmable valves. Chronic headaches are most often attributed to medical reasons (e.g. migraines, tension) and managed with patient reassurance. The most popular treatments for SVS include shunt revision (88%), cranial expansion (57%) and placement of an ASD (53%). SVS etiology was most often linked to early onset of shunting, chronic overdrainage and/or loss of brain compliance.

**Conclusions:** This survey shows discrepancies in shunt-dependent hydrocephalus understanding and management style among a representative group of experienced North American pediatric neurosurgeons. In particular, there are differing opinions regarding the primary cause of ventricular shunt obstructions and the origins of SVS. However, there appears to be general consensus in approach and management of overdrainage and chronic headaches. These results provide impetus for better studies evaluating the pathophysiology and prevention of shunt obstruction and SVS.

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#### O36

##### The risk of ventricular catheter misplacement and intracerebral hemorrhage in shunt surgery for hydrocephalus

Linus Hultegård<sup>1</sup>, Asgeir Jakola<sup>1,2</sup>, Dan Farahmand<sup>1,2</sup>

<sup>1</sup>University of Gothenburg, Sweden; <sup>2</sup>Institute of Neuroscience and Physiology at Sahlgrenska Academy, Sweden

E-mail: Linush@student.gu.se

*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:O36

**Introduction:** Communicating hydrocephalus is caused by an accumulation of cerebrospinal fluid (CSF) that is often treated with a ventricular shunt. There are few studies on the rates of ventricular catheter (VC) misplacement and postoperative intracerebral hemorrhage (ICH) after shunt surgery. In this study, we evaluated the rate of VC misplacement and ICH after shunt surgery. In addition, VC misplacement was correlated to postoperative ICH and shunt revision within six months, respectively.

**Methods:** All patients (n=245) that received a ventriculoperitoneal or ventriculoatrial shunt during January 2012 and December 2014 at the department of neurosurgery at Sahlgrenska University Hospital, Gothenburg, Sweden were included in the study. Patients who did not undergo postoperative imaging (n=14) were excluded. Misplacement was defined as when the tip of the VC was located in the contralateral ventricle or intraparenchymatously. The event of ICH was based on verification of intraparenchymatous blood on an early (<48 h) head CT postoperatively. The shunt revision rate within six months postoperatively was compared between patients with and without misplacement of the VC.

**Results:** Misplacement of the VC tip was found in 77 patients (33%); 71 patients with the VC tip in the contralateral ventricle and 6 patients with the VC tip intraparenchymatously. Nine patients (4%) had postoperative ICH verified by imaging of which five (56%) patients had a misplacement of the VC. The revision rate for accurately placed VCs was 17 % compared to 21 % for misplaced VC (n.s.).

**Conclusions:** Misplacement of the VC occurred in one third of the shunt insertions; however this did not significantly increase the shunt revision rate. The study showed a fairly high rate of radiologically verified ICH, particularly when the VC was misplaced intraparenchymatously.

### O37

#### Clinical signs and symptoms of adult patients with intracranial arachnoid cysts

Katrin KM Rabie<sup>1</sup>, Roberto Doria Medina, Mats Högfeldt, Per Hellström, Carsten Wikkelsö, Magnus Tisell  
Hydrocephalus research unit, Institution of Neuroscience, Sahlgrenska Academy, Sweden  
E-mail: katrinrabie@gmail.com  
Fluids and Barriers of the CNS 2015, 12(Suppl 1):O37

**Background:** Patients with arachnoid cysts have a wide range of symptoms from asymptomatic to a variety of symptoms and signs. Indication for surgical treatment can be challenging in case of the most common symptoms; headache and vertigo which are both subjective and common. The aim of this prospective study was to describe variety of symptoms in relation to cyst location and volume and their response to treatment.

**Methods:** 112 adults 46,6 y (18-77 y) with de novo cysts were prospectively included and evaluated through our hydrocephalus research unit with extensive test battery including neurological-, neuropsychological-, motor function testing and MRI. After evaluation, 76 patients were offered surgery. 54 accepted and 22 declined. 33 patients were regarded asymptomatic. Operated patients were followed up 3 months after surgery with the same test battery. Cyst volume was measured with OsiriX<sup>®</sup> software.

**Results:** There was no significant difference in MMSE, frequency of head trauma or length of education between operated patients, those who declined or were asymptomatic. Asymptomatic patients had a significantly lower cyst volume, 18 ml (1-88), compared to those who were offered surgery 47 ml (3-223). Headache and dizziness was as prevalent in asymptomatic patients as the operated ones. In operated patients, headache improved significantly ( $p<0,05$ ) 3 months after surgery. Cyst volume reduced to 31 ml (0-282,  $p<0,001$ ) 3 months after surgery. Cyst volume reduced further to 29 ml (0-279,  $p<0,001$ ) 1 year postoperatively. 43 patients considered themselves improved in at least one major symptom after 3 months. 9 patients were the same and 2 worse. In 22 (41%) patients at least one major symptom ceased completely. Clinical and radiological improvement did not correlate.

**Conclusion:** 80% of patients experienced an improvement in at least one major symptom 3 months after surgery. Clinical improvement did not correlate with reduction in cyst volume.

### O38

#### Magnetic resonance elastography demonstrates increased brain stiffness in normal pressure hydrocephalus

John Huston<sup>1</sup>, Avital Perry, Nikoo Fattahi, Arvin Arani, Fred Meyer, Richard Ehman  
Mayo Clinic, USA  
E-mail: jhuston@mayo.edu  
Fluids and Barriers of the CNS 2015, 12(Suppl 1):O38

**Introduction:** Normal pressure hydrocephalus (NPH) is a potentially reversible cause of ventriculomegaly characterized by a classic triad of gait disturbance, cognitive impairment and urinary incontinence in older adults. Shunt tube placement is currently the mainstay therapy for NPH. However, unpredictable therapeutic responses as well as associated surgical complications necessitate better characterization of surgical candidates. The purpose of this study was to use MR Elastography (MRE) to determine brain tissue stiffness and outcomes after shunting in NPH patients compared with age and sex matched healthy controls.

**Methods:** With IRB approval 10 patients (age range of 67-79 years) with NPH who were scheduled for ventriculoperitoneal shunting underwent preoperative MRE and were correlated with 21 age- and sex-matched normal controls (age range of 67-80 years). Studies were performed on a 3T scanner with a single-shot spin-echo EPI pulse sequence. Shear waves were introduced into the brain through an external source of vibration using a frequency of 60 Hz. We calculated the elasticity of different regions of interest (ROI) in the brain including the whole brain excluding the cerebellum (cerebrum), frontal, temporal, parietal, occipital lobes, deep grey matter/ white matter and the cerebellum. Associations between ROIs

and symptoms were evaluated including cognitive decline, urinary incontinence, gait disturbance, duration of symptoms, opening pressure, improvement after lumbar puncture, and postoperative improvement. Statistical analysis included t test and linear regression.

**Results:** MRE demonstrated significantly increased parenchymal stiffness among NPH patients as compared to normal controls in multiple ROIs, including the cerebrum, occipital, and parietal lobes ( $p=0.042$ ,  $p=0.002$ ,  $p=0.011$  respectively). Postoperative improvement was associated with significant increased stiffness in deep grey/white matter, whereas postoperative failure was associated with significant increased temporal lobe stiffness ( $p=0.013$ ,  $p=0.012$ ).

**Conclusions:** Brain MRE of patients with NPH revealed increased stiffness of the cerebrum, occipital and parietal lobes with a significant association between a range of NPH symptoms including the classic clinical triad with increased parenchymal stiffness. Surgically-responsive NPH was significantly associated with deep grey/white stiffness. MRE may guide selection of patients for shunting in the setting of equivocal diagnoses of NPH.

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### O39

#### Epidemiological characteristics of patients with idiopathic normal pressure hydrocephalus in Japan: analysis of the treatment

Madoka Nakajima<sup>1</sup>, Masakazu Miyajima, Chihiro Akiba, Ikuko Ogino, Hajime Arai  
Juntendo University School of Medicine, Japan  
E-mail: madoka66@juntendo.ac.jp  
Fluids and Barriers of the CNS 2015, 12(Suppl 1):O39

**Introduction:** To clarify the epidemiological and clinical characteristics of idiopathic normal pressure hydrocephalus (iNPH) in Japan, a nationwide epidemiological survey was conducted, focusing on treatment analysis.

**Methods:** Study participants were selected according to hospital bed capacity, using a random sampling method. In a primary survey, the number of iNPH patients in each hospital department during the year 2012 was estimated for stratification of institutions and next, in a secondary survey, selected patients provided detailed information, determining the clinical and epidemiological features of interest.

**Results:** In the primary survey 1804 clinical departments responded (recovery rate: 42.7% ) for 3079 individuals, including 1815 individuals who underwent shunt surgery. The estimated annual number of patients receiving treatment was 13,000 (95% CI: 10000 to 16000). The estimated prevalence rate for hospital-based patients in 2012 was 10.2 individuals per 100,000.

Analyses were conducted on 1495 respondents (885 males (59.2%): age 77.9±6.30(SD) years; and 610 females (40.8%): age 78.0±6.41 years. Results showed 992 iNPH patients (66.1%) treated with shunt surgery, 547 patients (77.6±6.12yo) with lumboperitoneal (LPS), 428 patients (76.51±6.19yo) with ventriculoperitoneal (VPS) and 17 with ventriculoatrial (VAS) shunting. Four patients having both LPS and VPS.

In 120 out of 992 shunted patients were recorded complications (12.1%), including 77 out of 547 patients with LPS and 43 out of 428 patients with VPS, without statistically significant difference between the two subgroups ( $p=0.092$ ).

Therapeutic efficacy exceeded 90% with improvement of 1 point or higher on the modified Rankin Scale (mRS) in 56%. Age and Alzheimer's Disease were factors with a negative impact on the therapeutic prognosis, with odds ratio of 1.029 95%CI (1.013-1.047)  $p=0.001$ , and 1.365 95% CI (1.008-1.849)  $p=0.044$ , respectively. They had significant impact on the prognosis of improvement according to mRS.

**Conclusions:** We reported hospital based survey study in Japan, providing the main characteristics of iNPH epidemiology and management for 2012.

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## O40

### Comparison between pre-operative MRI and intra-operative endoscopic findings for idiopathic normal pressure hydrocephalus

Daisuke Kita<sup>1,2\*</sup>, Yasuhiko Hayashi<sup>2</sup>, Issei Fukui<sup>2</sup>, Masahiro Oishi<sup>2</sup>, Cheho Park<sup>1</sup>, Mitsutoshi Nakada<sup>2</sup>

<sup>1</sup>Department of Neurosurgery, Noto General Hospital, Japan; <sup>2</sup>Department of Neurosurgery, Kanazawa University, Japan

E-mail: kitad@med.kanazawa-u.ac.jp

*Fluids and Barriers of the CNS* 2015, **12**(Suppl 1):O40

**Introduction:** Endoscopic examination of the intra-ventricular walls is rarely performed for cases of idiopathic normal pressure hydrocephalus (iNPH) since shunting is the first treatment option for iNPH. We conducted intra-operative endoscopy during shunt surgery in patients with iNPH and compared the findings with their pre-operative MRI data.

**Methods:** Eleven patients (6 men and 5 women, age range: 67-84 years, mean age: 75.5 years) with probable iNPH consistent with the Japanese iNPH guideline were included in this study. High-resolution MRI (T1-3D-SPGR or FIESTA) was conducted pre-operatively. Intra-ventricular observations were performed with a flexible endoscope, Olympus VEF-type V, via a frontal burr hole during shunt surgery. Student's t-test and Fisher's direct method were employed for statistical analyses.

**Results:** Laceration of the septum pellucidum was found in 4 patients (36.3%) by direct endoscopic observations. The foramen of Monro and Sylvian aqueduct were not stenosed in any case, as revealed both radiologically and endoscopically. For all cases, downward ballooning of the third ventricle floors was not observed in pre-operative MRIs, while thin third ventricular floor and lamina terminalis were observed in intra-operative endoscopic views. The interspace between the bilateral mammillary bodies varied from being wide to narrow, as revealed by endoscopy. A significant correlation was found between laceration of the septum pellucidum and the callosal angle measured by MRI ( $104 \pm 5.77$  degrees for lacerated vs.  $70.3 \pm 7.44$  degrees for non-lacerated,  $p < 0.001$ ). Width of the third ventricle and that of the interspace between the bilateral mammillary bodies showed a non-significant correlation ( $14.2 \pm 1.86$  for widely opened vs.  $11.7 \pm 2.49$  for narrowly closed,  $p = 0.052$ ).

**Conclusion:** In iNPH, the pre-operative MRI findings of dull callosal angle and wide third ventricle were closely related to the intra-operative endoscopic findings of laceration of the septum pellucidum and wide opening between the bilateral mammillary bodies, respectively.

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## O41

### Cardiovascular risk factors are associated with Idiopathic Normal Pressure Hydrocephalus

Hanna Israelsson<sup>1\*</sup>, Bo Carlberg<sup>2</sup>, Carsten Wikkelso<sup>3</sup>, Katarina Laurell<sup>1</sup>, Babar Kahlon<sup>4</sup>, Anders Eklund<sup>5</sup>, Jan Malm<sup>1</sup>

<sup>1</sup>Department of Pharmacology and Clinical Neuroscience, Umeå University, Sweden; <sup>2</sup>Department of Public Health and Clinical Medicine, Umeå

University, Umeå, Sweden; <sup>3</sup>Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Sweden; <sup>4</sup>Department of Neurosurgery, Lund University, Lund, Sweden; <sup>5</sup>Department of Radiation Sciences, Umeå University, Umeå, Sweden

E-mail: hanna.israelsson@neuro.umu.se

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**Introduction:** An emerging concept is a possible association between vascular disease/cardiovascular risk factors (CVRF) and idiopathic normal pressure hydrocephalus (INPH). However, the CVRF profile of INPH has not been investigated using a modern epidemiological approach. The objective for this case-control study was to determine the total CVRF profile in a large cohort of shunted INPH-patients, compared to the population.

**Material – method:** INPH patients consecutively shunted 2008-2010 in Sweden were scrutinized. Inclusion criteria were: 60-85 years and not having dementia, (i.e., mini mental state examination  $\geq 23$ ). Community-based controls were matched to the patients according to age and sex. All participants completed an extensive questionnaire and had a visit to their health-care giver for blood samples, electrocardiogram and anthropometrical measurements. Investigated VRF were: hypertension, hyperlipidemia (measured by apolipoprotein B and A1), diabetes, obesity, psychosocial factors (stress and depression), smoking, dietary pattern, alcohol intake, cardiac disease and physical activity. Cerebrovascular disease (CVD) and peripheral vascular disease (PVD) (claudicatio intermittens, kidney disease (measured by decreased renal function) and stenosis of the extracranial cerebral arteries) were also assessed.

**Results:** The study population consisted of 176 INPH patients (mean age 74 years  $\pm$  6SD, 42% females) and 368 controls (mean age 73 years  $\pm$  6SD, 37% females). In the multivariable logistic regression models, hyperlipidemia (OR: 2.380, 95% CI: 1.434-3.950); diabetes (OR: 2.169, 95% CI: 1.195-3.938); obesity (OR: 5.428, 95% CI: 2.502-11.772) and; psychosocial factors (OR: 5.343, 95% CI: 3.219-8.868) were independently associated with INPH. In addition, hypertension (OR: 1.656, 95% CI: 1.017-2.697) and physical inactivity (OR: 2.840, 95% CI: 1.709-4.719) were overrepresented in INPH. CVD were also overrepresented amongst the patients, as well as PVD.

**Conclusion:** CVRF are overrepresented amongst INPH patients compared to the population, and CVRF and subsequent vascular disease may contribute to the development of INPH. A more aggressive medical management of CVRF in INPH in addition to shunt surgery is probably needed.

## O42

### Is there an over-prescription of psychotropic drugs to patients with Idiopathic Normal Pressure Hydrocephalus?

Hanna Israelsson<sup>1\*</sup>, Per Allard<sup>2</sup>, Anders Eklund<sup>3</sup>, Jan Malm<sup>1</sup>

<sup>1</sup>Department of Pharmacology and Clinical Neuroscience, Umeå University, Umeå, Sweden; <sup>2</sup>Department of Clinical Science, division of Psychiatry, Umeå University, Umeå, Sweden; <sup>3</sup>Department of Radiation Sciences, Umeå University, Umeå, Sweden

E-mail: hanna.israelsson@neuro.umu.se

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**Introduction:** Over-prescription of psychotropic drugs among elderly and cognitively impaired individuals is a well-known problem. One common side effect to a majority of these drugs is an increased risk to fall. This may be fatal in a population already susceptible for falling, such as INPH patients. The objective of this study was to describe the prevalence of prescribed antidepressants, antipsychotics, anxiolytics, hypnotics, and sedatives in shunted INPH patients compared with the population.

**Method:** INPH patients consecutively shunted 2008-2010 in Sweden were scrutinized in one to three years after shunt surgery (in 2011) and patients remaining after inclusion (within 60-85 years and not having dementia, i.e., mini mental state examination  $\geq 23$ ) had a standardized visit to their health-care giver and answered a questionnaire. Age- and sex-matched population-based controls underwent the same procedure. The prescription of psychotropic drugs and psychiatric diagnoses were obtained from the registers of the Swedish National board of Health and Welfare, where all diagnoses and prescribed medication are registered for all individuals receiving medical care in Sweden.



**Results:** The study population consisted of 176 INPH patients and 368 controls. More INPH patients than controls received antidepressants (30% vs 11%,  $p < 0.001$ ). However, there was no difference between INPH patients and controls regarding a verified diagnosis of depression (2% vs 1%,  $p = 0.40$ ). More INPH patients than controls received anxiolytics, hypnotics, and sedatives (34% vs 25%,  $p = 0.027$ ). There was no difference between INPH patients and controls regarding antipsychotics (2% vs 1%).

**Conclusion:** INPH patients received antidepressants, anxiolytics, hypnotics and sedatives in a higher degree than the general population despite the lack of a definitive psychiatric diagnosis. Considering the possible serious adverse effects of psychotropic drugs in cognitively impaired elderly, it is important to ensure that the prescribed medications are both adequate and safe when releasing an INPH patient from the hospital after shunting.

#### O43

##### Familial idiopathic normal pressure hydrocephalus

Joel Huovinen<sup>1\*</sup>, Sami Kastinen<sup>1</sup>, Simo Komulainen<sup>1</sup>, Minna Oinas<sup>2</sup>, Cecilia Avellan<sup>2</sup>, Janek Franzen<sup>3</sup>, Jaakko Rinne<sup>3</sup>, Antti Ronkainen<sup>4</sup>, Mikko Kauppinen<sup>5</sup>, Kimmo Lönnroth<sup>6</sup>, Markus Perola<sup>7</sup>, Okko T Pyykkö<sup>1</sup>, Anne M Koivisto<sup>8</sup>, Anne M Remes<sup>8</sup>, Mikko Hiltunen<sup>8,9</sup>, Seppo Helisalmi<sup>8</sup>, Mitja Kurki<sup>1,10</sup>, Juha E Jääskeläinen<sup>1</sup>, Ville Leinonen<sup>1</sup>

<sup>1</sup>Department of Neurosurgery, Kuopio University Hospital and Neurosurgery, Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland;

<sup>2</sup>Department of Neurosurgery, University of Helsinki and Helsinki University Hospital, Finland; <sup>3</sup>Clinical Neurosciences, Department of Neurosurgery, Turku University Hospital, Turku, Finland; <sup>4</sup>Department of Neurosurgery, Tampere University Hospital, Tampere, Finland; <sup>5</sup>Department of Neurosurgery, Oulu University Hospital, Oulu, Finland; <sup>6</sup>South Ostrobothnia Central Hospital, Seinäjoki, Finland; <sup>7</sup>National Institute for Health and Welfare, Finland and University of Helsinki, Helsinki, Finland; <sup>8</sup>Unit of Neurology, Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland and Department of Neurology, Kuopio University Hospital, Kuopio, Finland;

<sup>9</sup>Institute of Biomedicine, University of Eastern Finland, Kuopio, Finland;

<sup>10</sup>Analytical and Translational Genetics Unit, Department of Medicine, Massachusetts General Hospital, USA, Program in Medical and Population Genetics, Broad Institute of MIT and Harvard, USA Stanley Center for Psychiatric Research  
E-mail: jhuovine@student.oulu.fi

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**Introduction:** Idiopathic normal pressure hydrocephalus (iNPH) is a late-onset, surgically alleviated, progressive neurodegenerative disease with unknown etiology. There are few studies describing pedigrees with multiple affected relatives. Our aim was to identify and characterize a potential familial subgroup of idiopathic normal pressure hydrocephalus in a nation-wide Finnish cohort.

**Methods:** Overall 375 iNPH-patients operated between 1993 and 2014 were questioned and phone interviewed, whether they have relatives with either diagnosed iNPH or disease-related symptomatology. Genograms of families with such findings were drawn.

**Results:** 60 patients (16 %) had potential familial iNPH. 18 patients from 12 separate pedigrees had at least one relative shunted due to iNPH. Patients with familial iNPH reported a complete triad of NPH-symptoms ( $p = 0.03$ ) and memory problems ( $p = 0.014$ ) more often than sporadic cases. Both shunted and symptomatic relatives were mainly first-degree.

According to age-adjusted multivariate logistic regression analysis diagnosed dementia (odds ratio [OR] 2.9; 95% confidence interval [CI], 1.5–5.4) and nonarthritic rheumatoid etiologies (OR, 4.4; 95% CI, 1.6–11.7) were more frequent in familial than sporadic patients. Geographical variation in the occurrence of iNPH was observed, the incidence being highest in Eastern Finland. Frequency of APOE epsilon 4 as well as diagnosed Alzheimer's disease (AD) and AD-medication were similar in familial and sporadic iNPH-patients.

**Conclusions:** This study indicates a familial entity of iNPH offering a novel approach to discover the potential genetic characteristics of iNPH. Furthermore, these pedigrees offer an intriguing opportunity to conduct longitudinal studies focusing on potential preclinical signs of iNPH. Our findings support iNPH as a specific neurodegenerative disease.

#### O44

##### Diagnostic Assessment of Adult Hydrocephalus Log compared to standard normal pressure hydrocephalus diagnostic tools

Ignacio Jusue-Torres<sup>1\*</sup>, Jennifer Lu<sup>1</sup>, Jamie Robison<sup>1</sup>, Jamie Hoffberger<sup>1</sup>, Jan Wemmer<sup>1</sup>, Abanti Sanyal<sup>2</sup>, Daniele Rigamonti<sup>1</sup>

<sup>1</sup>Johns Hopkins University, School of Medicine, Department of Neurosurgery, USA;

<sup>2</sup>Johns Hopkins University, Bloomberg School of Public Health, Department of Biostatistics, USA

E-mail: jusuet1@jhmi.edu

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**Introduction:** Early treatment in Normal Pressure Hydrocephalus (NPH) yields better post-operative outcomes. Our current tests often fail to detect significant changes at early stages. We developed a new scoring system (LP log score) and sought a "proof of concept" that this tool is more sensitive in detecting clinical differences than the current ones.

**Methods:** We prospectively studied 62 consecutive new patients with suspected idiopathic NPH. Secondary, previously treated and obstructive cases were not included. We collected age, pre and post Lumbar Puncture (LP) Tinetti, Timed Up and Go (TUG), European NPH scale and LP log scores. LP log score is recorded at baseline and for 7 consecutive days after removing 40 cc of CSF via LP. We studied the diagnostic accuracy of the tests for surgical indication.

**Results:** Median age at presentation was 76 (71-80) years old. TUG ( $p < 0.0001$ ) and Tinetti ( $p < 0.0001$ ) showed significant differences between presentation and post-LP scores. PostLP Log showed improvement in 90% of people with good baseline TUG, Tinetti and MCV tests and in 93% of people who did not show any pre-post LP change in TUG, Tinetti and MCV grade. Sensitivity, Specificity, and Accuracy to detect intention to treat when positive postLP improvements were respectively 4%, 100% and 24% for TUG, 21%, 86%, 34% for Tinetti, 66%, 29% and 58% for MCV grade and 98%, 33% and 85% for LP log. PreLP-postLP TUG improvement and preLP-postLP Tinetti improvement were not associated with surgical indication ( $p > 0.05$ ). LP log improvement was associated with surgical indication OR: 24.5 95%CI (2.4-248.12) ( $p = 0.007$ ).

**Conclusions:** LP log showed a higher sensitivity and diagnostic accuracy detecting clinical differences in NPH than the current diagnostic approach. Our next step is to conduct a cross-validation analysis of the diagnostic and prognostic accuracy of this new tool.

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#### O45

##### Predicting neuropsychological outcome following shunt operation in iNPH using reliable change indices (RCIs)

Maria Wallin<sup>\*</sup>, Mats Tullberg, Carsten Wikkelso, Per Hellström  
Hydrocephalus research unit at the institute of neuroscience and physiology, Sweden

E-mail: maria.a.wallin@vgregion.se

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**Introduction:** While most INPH patients experience a change in neuropsychological functioning after shunt operation there is a considerable variation in the extent, direction and nature of change. In this study we examined preoperative characteristics and their relationship to neuropsychological preoperative functioning and postoperative change. To determine neuropsychological change, reliable change indices (RCIs) were used. RCIs have been used to identify cognitive changes in other populations such as epilepsy, Parkinson's disease, dementia and sports medicine but have never previously been used in INPH research. The aim of the study was to aid patients and healthcare professionals to make informed decisions regarding surgery and to introduce the use of RCIs to establish change after shunting.

**Methods:** Data from 290 consecutive patients with INPH that were referred to the Sahlgrenska university hospital INPH unit between 1999 and 2013 were included in the analysis. These patients had undergone a brief neuropsychological assessment pre- and postoperatively. The test battery consisted of Rey Auditory Verbal Learning Test, Grooved Pegboard and Stroop. RCIs were used to quantify change. Multiple regression analysis was used to examine the effects of age, sex, education, amount of sleep, vascular risk factors, gait, balance, paratonia, and continence on preoperative neuropsychological function and RCI.

**Results:** Improvement and deterioration in the different neuropsychological domains were determined using RCI with 80% confidence limit. The proportions of patients who improved were 26-47% and 6-18% deteriorated. The preliminary results show that patients with more pronounced preoperative INPH symptomatology and vascular risk factors had a lower neuropsychological level of functioning. Female patients and younger patients with higher education tended to show slightly better results. The correlations between preoperative characteristics and RCIs were modest.

**Conclusions:** RCI is a measurement that can detect and determine meaningful changes in INPH patients after shunting. The measure has been successfully used in several other areas to identify cognitive changes after treatment. The introduction of RCI in INPH research and clinical practice can improve the certainty of judgments pertaining to neuropsychological changes after shunting.

#### O46

##### **One-year outcome in patients with idiopathic normal-pressure hydrocephalus treated with a lumbo-peritoneal shunt (SINPHONI-2), compared to ventriculo-peritoneal shunt (SINPHONI) used as a historical control**

Masakazu Miyajima<sup>1\*</sup>, Hiroaki Kazui<sup>2</sup>, Etsuro Mori<sup>3</sup>, Masatsune Ishikawa<sup>4</sup>  
<sup>1</sup>Department of Neurosurgery, Juntendo University Graduate School of Medicine, Japan; <sup>2</sup>Department of Psychiatry, Osaka University Graduate School of Medicine, Japan; <sup>3</sup>Department of Behavioral Neurology and Cognitive Neuroscience, Tohoku University Graduate School of Medicine, Japan; <sup>4</sup>Normal-Pressure Hydrocephalus Centre, Otowa Hospital, Japan  
E-mail: mmasaka@juntendo.ac.jp

*Fluids and Barriers of the CNS* 2015, **12**(Suppl 1):O46

**Introduction:** Idiopathic normal pressure hydrocephalus (INPH) is treated with cerebrospinal fluid shunting, and ventriculo-peritoneal shunt (VPS) is the current standard treatment. The goal of this pooled analysis was to compare the efficacy and safety between VPS and lumbo-peritoneal shunt (LPS) in patients with INPH specified as disproportionately enlarged subarachnoid space hydrocephalus (DESH).

**Methods:** We conducted a multicenter prospective 3-month randomized controlled trial, and then a 1-year extension study, where all subjects received an LPS with a programmable valve and were examined periodically for 1 year. Eighty-three patients with INPH (60 to 85 years old) presenting with ventriculomegaly, high-convexity and medial subarachnoid space tightness in magnetic resonance imaging were recruited from 20 neurological or neurosurgical centers in Japan between March 1, 2010 and October 19, 2011. The primary outcome was the modified Rankin scale (mRS) score 1 year after surgery, and secondary outcome included the NPH grading scale (NPHGS). The VPS SINPHONI study was used as a historical control.

**Results:** The proportion of patients with a favorable outcome (i.e., improvement of at least one level in mRS) was 63% (95% CI: 51-73%), and was comparable to that with VPS implantation (69%, 95%

CI: 59-78%). In NPHGS, the one-year improvement rate was 75% (95% CI: 64-84%) and was comparable to that of VPS (77%, 95% CI: 68-84%). Serious adverse events (SAEs) occurred in 19 patients (22%), 10 of which were related to surgery. SAEs were more common with LPS than with VPS (15%).

**Conclusion:** Our results show that LPSs with programmable valves are effective for treating INPH as an alternative to VPSs.

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#### O47

##### **Risk factors for subdural hematomas in patients shunted for idiopathic normal pressure hydrocephalus**

Nina Sundström<sup>1\*</sup>, Johan Wallmark<sup>2</sup>, Anders Eklund<sup>1</sup>, Lars-Owe Koskinen<sup>3</sup>, Jan Malm<sup>2</sup>

<sup>1</sup>Department of Radiation Sciences, Biomedical Engineering, Umeå University, Umeå, Sweden; <sup>2</sup>Department of Clinical Neuroscience, Umeå University, Umeå, Sweden; <sup>3</sup>Department of Neurosurgery, Division of Pharmacology and Clinical Neuroscience, Umeå University, Umeå, Sweden  
E-mail: nina.sundstrom@vll.se

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**Introduction:** Subdural hematoma (SDH) is a common complication of shunt surgery, but it is not clear which are the most important underlying causes. Based on a large prospective population based material, the objective of this study was to identify the most important risk factors for postsurgical SDH in patients with idiopathic normal pressure hydrocephalus (INPH).

**Methods:** The Swedish Hydrocephalus Quality Registry (SHQR) is a prospective population based database in which hydrocephalus surgeries have been recorded nationwide since 2004. In this study, 1458 INPH patients shunted between 2004 and 2014 were included. Post surgery, 122 (8.4 %) developed SDH. The prevalence of risk factors for SDH was compared between patients with and without postoperative SDH (controls).

**Results:** Median time between surgery and SDH was 125 days. Men were predisposed for development of SDH (73 % males in the SDH group vs. 59.6 % in the control group,  $p=0.004$ ). Initial, as well as last shunt opening pressure (Popen) before SDH were lower in the SDH group compared to the controls (108.0 vs. 115.5 mmH<sub>2</sub>O ( $p=0.003$ ) and 98.8 vs. 107.5 mmH<sub>2</sub>O ( $p=0.006$ ) respectively). Antisiphoning devices (ASD) were used to the same extent in both groups. On average, Popen was 21.7 and 24.6 mmH<sub>2</sub>O lower in shunts with than without an ASD at time of surgery and last adjustment respectively. Despite this, the proportion of SDHs was the same in both groups. No differences were seen for adjustable vs. fixed valves, proximal catheter location, ASA physical status classification system score, Rankin scale score or co-morbidity.

**Conclusions:** Despite new shunt designs, SDH is still a common complication in patients shunted for iNPH. The predominant risk factors were found to be male sex and lower Popen. The complication was also related to the presence or absence of an ASD, since an ASD allowed for a lower Popen without an increased complication rate. This indicates that hydrodynamical issues play an important role in the development of SDH in iNPH patients. Thus, methods allowing individual adjustment of Popen are needed in order to optimize functional improvement and minimize the number of SDHs.

#### O48

##### Association between high biomarker probability of Alzheimer's disease and improvement of cognition and gait after shunt surgery in patients with idiopathic normal pressure hydrocephalus

Hiroaki Kazui<sup>1</sup>, Hideki Kanemoto, Yukiko Suzuki, Syunsuke Sato, Takashi Suehiro, Shingo Azuma, Kenji Yoshiyama, Toshihisa Tanaka  
Osaka University Graduate School of Medicine, Japan  
E-mail: kazui@psy.med.osaka-u.ac.jp  
*Fluids and Barriers of the CNS 2015, 12(Suppl 1):O48*

**Introduction:** In Alzheimer's disease (AD), the concentration of amyloid  $\beta$ 1-42 ( $A\beta$ 42) in cerebrospinal fluid (CSF) is low and that of total tau ( $t$ -tau) is high. We evaluated the relationship between high CSF biomarker probability of AD and improvement of cognition and gait after shunt surgery in idiopathic normal pressure hydrocephalus (iNPH).

**Methods:** The subjects of this study were 37 iNPH patients (75.7 $\pm$ 5.8 years, MMSE:22.2 $\pm$ 4.2) who showed improvement of one of the triad symptoms at least after shunt surgery. We classified the patients into 16 patients with and 21 patients without the combination of low  $A\beta$ 42 and high  $t$ -tau in CSF. We compared the improvement on cognitive and gait examinations 3 months after the shunt between the two groups with an analyses of covariance (ANCOVA), in which the score at 3 months after the shunt was entered in the model as a dependent variable, the baseline score as a covariate and the group as a categorical variable.

**Results:** In 37 iNPH patients, significant improvement 3 months after shunt surgery was shown in the Timed Up and Go test ( $p<0.001$ ), MMSE ( $p<0.001$ ), attention/concentration of the WMS-R ( $p=0.028$ ), and digit symbol substitution of the WAIS-III ( $p<0.001$ ), but not in delayed recall of the short story in the Rivermead behavioral memory test (RBMT) ( $p=0.46$ ). The ANCOVA revealed that the iNPH patients without high CSF biomarker probability of AD showed significantly greater improvement in the delayed recall of the RBMT 3 months after shunt surgery than those with high CSF biomarker probability of AD ( $p=0.017$ ). In addition, in the latter group, the change 3 months after the shunt was not significant ( $p=0.14$ ). The ANCOVA showed no significant differences in the improvement 3 months after the shunt surgery between the two groups on the other evaluations.

**Conclusion:** The delayed recall ability might not improve after shunt surgery in iNPH patients with AD pathology.

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#### O49

##### Final pressure setting of programmable valve in ventriculo-atrial shunt for idiopathic normal pressure hydrocephalus

Kiyoshi Takagi  
Chiba-Kashiwa Tanaka Hospital, Japan  
E-mail: ktakagi-nsu@umin.ac.jp  
*Fluids and Barriers of the CNS 2015, 12(Suppl 1):O49*

**Introduction:** A quick reference table for setting programmable pressure valves in patients with idiopathic normal pressure hydrocephalus (iNPH) has been proposed for ventriculo-peritoneal shunt (VP shunt) (Miyake et al. *Neurol Med Chir (Tokyo)* 48, 2008). Recommended pressure has strong correlation with body mass index (BMI). However, little is known about the ideal pressure setting for ventriculo-atrial shunt (VA shunt). The purpose of this paper is to show the final pressure setting in the iNPH patients with good outcome received VA shunts and to investigate the correlation between the final pressure setting and preoperative factors.

**Patients and Methods:** Eighty-four iNPH patients with good outcome (improved modified Rankin Scale , improved mini-mental state examination over 3, cease of urinary incontinence, or reduced care-giver's burden without improvement of modified Rankin Scale) at one year after VA shunts using programmable valve with anti-siphon device were the candidates of this study. Correlations between final pressure setting and BMI, body length, body weight, and preoperative cerebrospinal fluid (CSF) pressure measured by lumbar tap were investigated. Data were shown in mean  $\pm$  SD and statistically analyzed by calculating Pearson product-moment correlation coefficients and the significant level was set at  $p$  less than 0.05.

**Results:** Mean age was 77.6  $\pm$  6.1 years old (male : female = 48 : 36). Mean body length, body weight, and BMI were 157.2  $\pm$  8.8 cm, 54.1  $\pm$  10.8 kg, and 21.8  $\pm$  3.3 respectively. Preoperative CSF pressure was 118.9  $\pm$  34.2 mmH<sub>2</sub>O. The mean initial valve pressure setting was 126.3  $\pm$  17.6 mmH<sub>2</sub>O (median = 120 mmH<sub>2</sub>O) and the mean final pressure setting was 62.1  $\pm$  31.3 mmH<sub>2</sub>O (median = 55 mmH<sub>2</sub>O). There were no significant correlations between the final pressure setting and BL, BW, BMI, and CSF pressure. In 43 cases, final pressures were below 50 mmH<sub>2</sub>O including 23 cases with the lowest setting of 30 mmH<sub>2</sub>O.

**Discussion and conclusion:** This study clearly demonstrated that there were no preoperative determinants for the ideal setting of valve pressure in VA shunt. It also demonstrated that the final setting was unexpectedly low and it suggests the necessity of lower setting valve.

#### O50

##### Shunt surgery in iNPH patients is cost-effective – a cost-utility analysis in the Western Sweden setting

Mats Tullberg<sup>1\*</sup>, Jakob Petersen<sup>1</sup>, Josefine Persson<sup>2</sup>, Daniel Jaraj<sup>1</sup>, Kerstin Andrén<sup>1</sup>, Per Hellström<sup>1</sup>, Carsten Wikkelsö<sup>1</sup>, Åsa Lundgren-Nilsson<sup>1</sup>  
<sup>1</sup>Hydrocephalus Research Unit, The Sahlgrenska Academy, University of Gothenburg, Sweden; <sup>2</sup>Gothia Forum for Clinical Research, Sahlgrenska University Hospital, Sweden  
E-mail: mats.tullberg@neuro.gu.se  
*Fluids and Barriers of the CNS 2015, 12(Suppl 1):O50*

**Introduction:** Idiopathic normal pressure hydrocephalus (iNPH) is a treatable but underdiagnosed condition. The number of diagnosed patients will probably increase in the future which will increase costs and challenge allocation of resources. Shunt surgery is successful in most patients and we recently reported that 86% of operated patients improved their health related quality of life (HRQOL), almost to the same level as found in the normal population. However, the cost-effectiveness of treatment for iNPH has not been reported. The aim of this study was to simulate the long-term effects and costs of shunt surgery versus no treatment in iNPH in a Swedish setting.

**Methods:** The cost-utility analysis of shunt surgery was based on a decision-analytic Markov model adapted to Swedish circumstances. The effectiveness measure was quality-adjusted life years (QALYs) gained per patient. Costs were derived from the European iNPH Multicenter Study and data on costs of dementia disorders in Sweden reported by the National Board of Health and Welfare. Data from thirty-seven patients with iNPH

(median age 70 years, range 50-89 years) evaluated before and six months after surgery with the EQ-5D (EuroQol Group-5 Dimension health survey) was used to calculate quality adjusted life years (QALYs). Figures of prevalence, natural course of iNPH and transition probabilities were obtained from the literature. One-way sensitivity analysis and probabilistic sensitivity analysis were carried out to investigate the robustness of the model.

**Results:** The preliminary model showed that shunt surgery in iNPH resulted in a gain of 3.03 life years and 3.12 QALYs along with an incremental cost of approximately \$48,021 or £32,014. The incremental cost-effectiveness ratio (ICER) was estimated to \$15,550 or £10,000 per gained QALY.

**Conclusions:** From the preliminary result of the simulation model, it can be concluded that shunt treatment in iNPH is cost-effective. The estimated average ICER of £10,000 per gained QALY is below the UK National Institute for Health and Care Excellence (NICE) acceptance level of £20,000 for cost-effective interventions.

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#### O51

##### A genetic risk factor for idiopathic normal pressure hydrocephalus (iNPH)

Takeo Kato\*, Hidenori Sato, Yoshimi Takahashi  
Yamagata University School of Medicine, Japan  
E-mail: tkato@med.id.yamagata-u.ac.jp

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**Introduction:** Idiopathic normal pressure hydrocephalus (iNPH) is clinically important as a treatable gait disturbance and/or preventable dementia by shunt operation. iNPH usually occurs as a sporadic onset; however, genetic factor(s) is suggested to be involved in the pathogenesis of iNPH because of the presence of familial onset (two or more patients with NPH in a single family) of the disease, whose clinical and brain MRI features are indistinguishable from those of iNPH. Up to the present time, the genetic risk factor(s) for iNPH remains undetermined.

**Methods and Results:** We made a whole-genome analysis for copy number variations (CNV), using DNA from peripheral blood of 8 subjects with MRI-supported possible iNPH/AVIM and 110 healthy controls. As a result, 4 (50%) of the 8 subjects were found to have a segmental copy number loss within the SFMBT1 (Scm-like with four MBT domains protein 1) gene. The copy number loss was heterozygous, and occurred at the 12 kb region within intron 2 of the SFMBT1 gene. Such genetic change was detected in one (0.9%) of the 110 controls. Next, using qPCR, we examined 8 patients with definite iNPH, who were shunt-responsive, and found that five (63%) of the 8 patients had a copy number loss at the same locus of the SFMBT1 gene. Immunohistochemical examination of the normal human brain revealed that the SFMBT1 protein localized mainly in the arterial walls, the ependymal cells, and the epithelium of the choroid plexus, which play a crucial role in the secretion, flow, and absorption of cerebrospinal fluid.

**Conclusions:** The present study suggests that a copy number loss within the SFMBT1 gene may be a genetic risk factor for iNPH. Further studies on SFMBT1 will contribute to the elucidation of molecular basis of iNPH.

#### O52

##### DESH negative normal pressure hydrocephalus: can patients still benefit from shunt insertion?

Tarek Mostafa, Claudia Craven\*, Neekhil A Patel, Edward W Dyson, Samir A Matloob, Aswin Chari, Patricia Haylock-Vize, Simon D Thompson, Syed N Shah, Andrew R Stevens, Huan Wee Chan, Jinendra Ekanayake, Ahmed K Toma, Laurence D Watkins  
Victor Horsley Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, Queen Square, London, UK  
E-mail: claudia.craven@gmail.com

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**Introduction:** Selecting probable idiopathic normal pressure hydrocephalus (iNPH) patients for shunt insertion presents a challenge because of coexisting comorbidities and other conditions that could mimic NPH. The characteristic appearance of DESH (Disproportionately Enlarged Subarachnoid Space Hydrocephalus) on brain imaging has been shown to have a high positive predictive value in identifying shunt responsive iNPH patients (SINPHONI trial). However, the negative predictive value of this radiological sign was not clearly demonstrated.

**Methods:** A single centre retrospective study of probable iNPH patients, who underwent ventriculoperitoneal shunt insertion. Case notes were reviewed for clinical presentation, prognostic tests used and postoperative improvement. Shunt responsive iNPH patients were identified as those having objective improvement in their walking speed, neuropsychological assessment as well as subjective improvements in gait, continence and memory, one year post operatively. Preoperative images were reviewed for DESH sign (2 independent reviewers). Negative and Positive Predictive Values (NPV and PPV) of DESH sign were determined post analysis.

**Results:** A total of 103 probable iNPH patients were included (31 were DESH positive (30%) and 72 were DESH negative (70%)). A total of 78 patients showed measurable improvement 1 year post shunt insertion (76%); 24 (31%) of these patients were DESH positive and 54 (69%) were DESH negative ( $P = <0.001$ ). Therefore, the DESH sign had a PPV of 77% and a NPV of 25%.

**Conclusion:** In our data, the presence of DESH sign demonstrates a high positive predictive value of 77%, in agreement with SINPHONI trial data. However, it has shown a low negative predictive value. We conclude that probable NPH patients should not be excluded from having shunt insertion based on the presence of DESH sign alone.

**Abbreviations:** DESH: Disproportionately Enlarged Subarachnoid Space Hydrocephalus; NPH: Normal Pressure Hydrocephalus.

#### O53

##### Neuropsychological effects of shunting in iNPH – determining major and minor responses

Maria Wallin, Mats Tullberg, Carsten Wikkelsö, Per Hellström\*  
Institute of neuroscience and physiology, Sweden  
E-mail: per.hellstrom@vgregion.se

*Fluids and Barriers of the CNS* 2015, 12(Suppl 1):O53

**Introduction:** iNPH is characterized by a wide range of neuropsychological deficits. The severity of impairment is associated with that of gait, balance and continence disturbances, and correlations between results on disparate neuropsychological tests are far stronger than among healthy; a dedifferentiation of functions.

Following surgery, performance at group level, is significantly improved and remains stable for at least the first year of treatment. Importantly, however, shunted iNPH patients still perform well below normal levels.

The magnitude of change varies substantially, some patients showing only modest advances or even further deterioration, whereas others show considerable improvements on the majority or all administered tests.

In this study we compared patients belonging to these two extremes, aiming to predict neuropsychological benefits of surgery.

**Methods:** Consecutive iNPH patients (N=235) underwent pre- and postoperative assessments of learning (Rey Auditory Verbal Learning test; RAVLT), dexterity (Grooved pegboard), basic processing speed (Stroop, color naming task) and executive control (Stroop, interference task). For each test the patients were divided into four groups (Q1-Q4) according to the quartile limits of the distributions of Reliable Change Indices (RCIs).

Q1 and Q4, i.e. the least and the most improved, were compared with regard to preoperative characteristics pertaining to demography, other iNPH manifestations and other findings in neurological and physiotherapeutic examinations, and CSF dynamics. For each set of analyses they were also compared with regard to the changes (RCI scores) and postoperative performances on the remaining three tests.

**Results:** Patients who showed substantial positive changes in one neuropsychological function did so in the others as well, and vice versa. For learning and dexterity, neither demographic, nor clinical or CSF dynamics predicted changes following treatment. In the group who showed the greatest improvement of basic processing speed, preoperative gait disorders were more severe, and paratonia was more frequent than among the least improved. Those with greatest positive changes in executive control also had more severe gait disorders and more frequent paratonia, and, in addition, more marked problems with turning, balance and continence, and a lower general intellectual level.

**Conclusion:** Neuropsychological improvement following shunt treatment is consistent across functions. Statistically reliable and meaningful changes in learning and dexterity can not be predicted from demography, severity in other iNPH symptoms or CSF dynamics. Changes of basic processing speed and executive control, however, do appear possible to foresee on the basis of preoperative findings.

#### 054

##### Amyloid precursor like protein 1 in Idiopathic Normal Pressure hydrocephalus; expanding the knowledge of an altered amyloid metabolism

A Jeppsson<sup>1\*</sup>, M Hölta<sup>2</sup>, H Zetterberg<sup>2</sup>, K Blennow<sup>2</sup>, C Wikkelso<sup>1</sup>, M Tullberg<sup>1</sup>

<sup>1</sup>Hydrocephalus Research Unit, Institute of Neuroscience and Physiology, The Sahlgrenska Academy, University of Gothenburg, Sweden; <sup>2</sup>Clinical Neurochemistry Laboratory, Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, the Sahlgrenska Academy, University of Gothenburg, Sweden

E-mail: annajeppsson@neurophys.gu.se

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**Introduction:** It has been shown previously that iNPH patients do exhibit suppressed levels of amyloid- $\beta$  (A $\beta$ ) and the precursors soluble amyloid precursor protein  $\alpha$ -, and  $\beta$ - (sAPP $\alpha$ , sAPP $\beta$ ) in combination with depressed levels of tau proteins, both phosphorylated and total (t-tau, p-tau) and elevated levels of Neurofilament light protein (NFL). Expanding on this knowledge, we wanted to study if the changes seen in the amyloid processing pathways could be expanded to other fragments in the amyloid metabolism pathway.

**Methods:** This retrospective study consists of 20 patients diagnosed with iNPH at the hydrocephalus unit at Sahlgrenska University hospital. 20 neurologically healthy individuals, undergoing knee surgery serves as healthy controls. All patients were examined clinically prior to surgery and at 6 month follow-up by the iNPH scale. Lumbar puncture was performed prior to surgery. Chemical analyses performed at the Clinical Neurochemistry Laboratory at the Sahlgrenska University hospital determined levels of NFL, Amyloid  $\beta$  isoform 38, 40, 42, soluble amyloid precursor protein alpha and beta, Amyloid precursor like protein 1 fragment 25, 27, 28 and YKL40.

**Results:** We found a lowering of sAPP $\alpha$  (0.50), sAPP $\beta$  (0.43) A $\beta$ 38 (0.45), A $\beta$ 40 (0.48), A $\beta$ 42 (0.32) and of APLP1b28 (0.88) in iNPH patients in comparison with healthy controls (HC) in combination with an elevation of APL1b25 (1.20) and APL1b27 (1.24) (concentration in iNPH/concentration in HC). NFL was elevated at a trend level, and YKL40 was suppressed, also at a trend level.

**Conclusions:** Data on A $\beta$ 38, -40, -42 and sAPP $\alpha$  and - $\beta$  are confirmative of earlier results and might be a reflection of reduced periventricular metabolism and even disturbance of synaptic function. The increased levels of APL1b 25 and 27 might indicate a broader disturbance of the amyloid metabolism than previously thought. This new study might provide a piece in understanding the alteration of brain metabolism in patients with iNPH by the use of CSF biomarkers.

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#### 055

##### Prevalence of idiopathic normal pressure hydrocephalus - a pilot study in Jämtland, Sweden

Catherine Michelle Rosell<sup>1\*</sup>, Johanna Andersson<sup>1</sup>, Karin Kockum<sup>1</sup>, Otto Lilja-Lund<sup>1</sup>, Lars Söderström<sup>2</sup>, Katarina Laurell<sup>1</sup>

<sup>1</sup>Department of Pharmacology and Clinical Neuroscience, Unit of Research, Education and Development, Östersund, Umeå University, Sweden; <sup>2</sup>Unit of Research, Education and Development, Östersund Hospital, Region Jämtland Härjedalen, Sweden

E-mail: miro0024@student.umu.se

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**Introduction:** This pilot study was conducted to describe the prevalence, age and gender distribution of idiopathic normal pressure hydrocephalus (iNPH) in Jämtland, a Swedish county.

**Methods:** A total of 200 people over the age of 65 were randomly selected from the Swedish population registry and sent a simple questionnaire with questions regarding gait and balance disturbance, continence and/or cognitive impairment, i.e. the cardinal symptoms of iNPH. A total of 67 of the responding participants, with and without symptoms of iNPH were then selected to undergo a CT scan of the brain and clinical examination. iNPH was classified as "probable", "possible" or "unlikely" according to modified European guidelines. Hellströms iNPH scale (1) was used to measure the severity of symptoms in the domains of gait, neuropsychology, balance and continence.

**Results:** Out of 66 people, 8 (12 %) received the diagnosis "probable", 8 "possible" (12%) and 50 "unlikely" (66 %) iNPH, which indicates a prevalence of 4% for the diagnosis "probable" iNPH in the total population of 200. There was a statistical difference in gender distribution weighted towards men but not between the age groups 80+ vs <80, a result most likely due to the lower number of participants over 80 years of age. Those diagnosed as unlikely iNPH, had a significantly higher mean iNPH score (87), corresponding to less symptoms, than those with probable iNPH (62) (p= 0.01).

**Conclusion:** The prevalence of probable iNPH in the population of 65 years and older was found to be 4 % with a higher proportion of men than women being diagnosed. Although the severity of symptoms was related to the iNPH diagnosis, classification according to the European guidelines revealed some need for revision. The results of this pilot study will be confirmed in a larger sample of 1000 persons.

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#### 056

##### Intracranial pressure is a physiological stress that determines sympathetic nervous system activity

Eric Albert Schmidt<sup>1,2\*</sup>, Fabien Despas<sup>1,3</sup>, Anne Pavy Le Traon<sup>1,4</sup>, Marek Czosnyka<sup>5</sup>, John Douglas Pickard<sup>5</sup>, Kamal Rahmouni<sup>6</sup>, Atuk Pathak<sup>1,3</sup>, Jean Michel Senard<sup>1,3</sup>

<sup>1</sup>Institut National de la Sante et de la Recherche Médicale, UMR-1048, Institut des Maladies Métaboliques et Cardiovasculaires, Toulouse, France;

<sup>2</sup>Department of Neurosurgery and Institute for Neurosciences, CHU and Toulouse University, Toulouse, France; <sup>3</sup>Department of Clinical Pharmacology, CHU and Toulouse University, Toulouse, France; <sup>4</sup>Department of Neurology and Institute for Neurosciences, CHU and Toulouse University, Toulouse, France; <sup>5</sup>Academic Neurosurgery, Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK; <sup>6</sup>Departments of Pharmacology and Internal Medicine, University of Iowa Carver College of Medicine, Iowa City, Iowa, USA

E-mail: schmidt.e@chu-toulouse.fr

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**Introduction:** The interplay between CSF dynamics, intracranial pressure (ICP), arterial blood pressure (ABP) and sympathetic nervous system (SNS) remains poorly understood. We know that raised ICP reduces CPP (i.e. ABP-ICP) and blood delivery to the brain. Massive ICP rise is also known to produce an increase in ABP termed the Cushing response, a terminal event occurring in extreme pathological conditions of brainstem ischaemia leading to a sympatho-adrenal response. Hence the Cushing response is

not activated in a normal patient and is not involved in the pathophysiology of NPH. However, it is still debated whether the Cushing response is an acute pathological response to brain ischemia or part of an important physiological reflex mechanism. Indeed clinical and experimental studies suggest that modest ICP increase modulates systemic hemodynamics probably via the SNS. We hypothesize that modest ICP changes drive sympathetic activity. Using state-of-the-art technique to measure SNS, we performed two different sets of experiments in humans and mice. In both species during controlled hydrostatic modest ICP increase and decrease, SNS was measured directly by microneurography and indirectly by heart rate variability analysis (HRVA).

**Methods:** In 10 patients suspected of NPH, ICP was measured and increased during lumbar infusion study. HR and ABP were non-invasively monitored. Muscle sympathetic nerve activity (MSNA) was recorded. In 15 anesthetized mice, ICP was measured and intraventricular infusion was performed. HR and ABP were invasively monitored. Renal sympathetic nerve activity (RSNA) was recorded. In human and mice, HRVA allows calculation of indices gauging sympathetic and parasympathetic indices.

**Results:** In humans, modest increase in ICP was associated with a parallel increase in MSNA (e.g. 7 mmHg ICP rise increases SNS-activity by 17%). ABP was stable. Similarly in mice, modest rise in ICP increased RSNA. In both species ICP drop significantly reduced MSNA and RSNA. HRVA confirmed that modest rise in ICP augments sympathetic indices in humans and mice.

**Conclusions:** Using gold-standard measurement of SNS, we demonstrate in both species that ICP drives efferent SNS outflow. ICP is not only a determinant of CPP but also a physiological stressor that influences and reversibly modulates SNS activity, even at relatively low values. We demonstrate a new physiological link between ICP and SNS activity which may represent an important highly regulated circuit. Our findings strongly suggest the presence of a novel intracranial baroreflex. It represents a paradigm shift in physiology of the heart-brain cross-talk and in the pathophysiology of hydrocephalus. CSF related diseases might participate to sympathetically-driven medical disorders.

## O57

### Association between inflammatory extension and the ventricular size in adult chronic communicating hydrocephalus: An experimental model of adult hydrocephalus

Ignacio Jusue-Torres<sup>1\*</sup>, Jennifer Lu<sup>1</sup>, Eric W Sankey<sup>1</sup>, Tito Vivas-Buitrago<sup>1</sup>, Joshua Crawford<sup>2</sup>, Mikhail Pletnikov<sup>2</sup>, Jiadi Xu<sup>3</sup>, Ari Blitz<sup>4</sup>, Barbara Crain<sup>5</sup>, Alicia Hulbert<sup>6</sup>, Hugo Guerrero-Cazares<sup>1</sup>, Oscar Gonzalez-Perez<sup>7</sup>, Alfredo Quiñones-Hinojosa<sup>1</sup>, Pat McAllister<sup>8</sup>, Daniele Rigamonti<sup>1</sup>

<sup>1</sup>Johns Hopkins University, School of Medicine, Department of Neurosurgery, USA; <sup>2</sup>Johns Hopkins University, School of Medicine, Department of Psychiatry and Behavioral Sciences, USA; <sup>3</sup>Johns Hopkins University, School of Medicine, F. M. Kirby Research Center for Functional Brain Imaging at the Kennedy Krieger Institute, USA; <sup>4</sup>Johns Hopkins University, School of Medicine, Department of Radiology and Radiological Science, USA; <sup>5</sup>Johns Hopkins University, School of Medicine, Department of Pathology, Division of Neuropathology, USA; <sup>6</sup>Johns Hopkins University, School of Medicine, Department of Oncology, USA; <sup>7</sup>University of Colima, Facultad de Psicología, Laboratorio de Neurociencia, Mexico; <sup>8</sup>Washington University, School of Medicine in St Louis, Department of Neurosurgery, USA  
E-mail: jusuet1@jhmi.edu

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**Introduction:** The pathogenesis of normal pressure hydrocephalus (NPH) is not fully understood and the relationship between inflammatory reaction extension and the ventricular enlargement is unknown.

**Methods:** Bilateral subarachnoidal injection of kaolin was administered in the cranial convexities of 20 adult rats. MRI was obtained using a Bruker Biospec 11.7 T MRI scanner at 14, 60, 90 and 120 days post kaolin injection. Radiological kaolin extension was defined by the number of kaolin locations showed in the MRI studies. At the end of the experiment, the heads of the rats were decalcified and sliced along with the skull in order to preserve the meninges and bone. A blinded neuropathologist studied the anatomical preparations and analyzed kaolin extension and the inflammatory and fibrotic response.

**Results:** Radiological ventricular size showed progressive growth over time at all times ( $p < 0.0001$ ). The fastest ventricular enlargement

happened within the first 2 months. Pathological specimens revealed kaolin location at the subarachnoidal space. The extension of the kaolin migration was heterogeneous among rats. Inflammatory and fibrotic response was present at the cranial convexities in all rats, adjacent to superior sagittal sinus in 94% rats, at the interhemispheric fissure in 56% rats, at the Olfactory Bulb in 61% rats, at the anterior basal cisterns in 72% rats, supracerebellar in 56% rats, at the quadrigeminal cisterns in 61% rats, at the lateral midbrain cisterns in 50% rats and within the Virchow-Robin spaces in 61% rats. The extension of the inflammatory response in the subarachnoidal space was associated with ventricular size ( $p = 0.02$ ), and the rate of ventricular enlargement ( $p = 0.03$ ).

**Conclusions:** The extension of the inflammatory response to kaolin injected in the subarachnoidal space is associated with ventricular size and the rate of ventricular enlargement in adult rats.

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## O58

### Exercise-induced changes of CSF vascular endothelial growth factor in adult chronic hydrocephalus patients

Mark Gregory Luciano<sup>1\*</sup>, Jun Yang<sup>1</sup>, Kaitlyn J Shanahan<sup>1</sup>, Leah P Shriver<sup>2</sup>  
<sup>1</sup>Cleveland Clinic, USA; <sup>2</sup>University of Akron, Depts. Chemistry and Biology, USA

E-mail: mark.luciano.md.phd@gmail.com

Fluids and Barriers of the CNS 2015, 12(Suppl 1):O58

**Background:** Vascular endothelial growth factor (VEGF) is a growth factor demonstrated to play a key role in cerebral angiogenesis and neurogenesis. It has been considered a critical component in hippocampus neurogenesis and memory formation and has been observed to increase in the rat hippocampus after exercise. In a previous study, we found increases in VEGF receptor and/or ligand in an experimental model of chronic e hydrocephalus in several brain areas and cerebrospinal fluid (CSF), suggesting a role in the adaption to chronic hypoxia. Here we investigate the ability of moderate exercise to increase CSF-VEGF levels in adult chronic hydrocephalus patients.

**Methods:** Lumbar CSF samples were collected from 17 normal pressure hydrocephalus (NPH) patients over 5 hours in 1-h intervals. During CSF collection, 11 patients (exercise group) underwent a standard in-room physical therapy session; 6 patients (no-exercise group) did not undergo a physical therapy session. CSF-VEGF levels were evaluated for increase related to exercise and the clinical response to CSF drainage.

**Results:** CSF-VEGF levels in the exercise group demonstrated significant increases 1-3hrs post-exercise compared with the levels 1-2hrs pre-exercise ( $p = 0.04$ ), and also showed significantly higher levels than the no-exercise groups ( $p = 0.03$ ). While patients who clinically improved with CSF removal did not demonstrate an increase in CSF-VEGF levels, those who did not clinically improve had higher CSF-VEGF levels after exercise. The post-exercise CSF-VEGF level in the group that did not clinically improve was significantly higher than both their own pre-exercise level ( $p = 0.02$ )

and also higher than that seen in the clinically improving group ( $p=0.05$ ) after exercise.

**Conclusions:** CSF-VEGF levels can increase after moderate exercise even in elderly hydrocephalus patients. This suggests a potential benefit of exercise in benefiting some of these patients may exist via a central VEGF mechanism. Increased VEGF levels after exercise in patients who showed no improvement with CSF drainage suggest that vascular injury may play a role in this group's pathophysiology.

## O59

### Decorin reduces white matter pathology in experimental hydrocephalus: a diffusion tensor imaging and immunohistochemical study

James Patterson McAllister<sup>1,3\*</sup>, Anuriti Aojula<sup>2</sup>, Hannah Botfield<sup>2</sup>, Osama Abdullah<sup>3</sup>, Ana Maria Gonzalez<sup>2</sup>, Dustin Ragan<sup>1</sup>, Ann Logan<sup>2</sup>, Alexandra Sinclair<sup>2</sup>

<sup>1</sup>Neurosurgery, Washington University School of Medicine, USA;

<sup>2</sup>Neurotrauma and Neurodegeneration, School of Clinical and Experimental Medicine, University of Birmingham, UK; <sup>3</sup>Bioengineering, University of Utah, USA

E-mail: pat.mcallister@wustl.edu

Fluids and Barriers of the CNS 2015, 12(Suppl 1):O59

**Introduction:** We have shown previously that Decorin, by antagonizing TGF- $\beta$ -mediated subarachnoid fibrosis, prevents ventriculomegaly in experimental juvenile hydrocephalus. To focus on white matter alterations, we sought to correlate cytopathological changes induced by hydrocephalus with diffusion tensor imaging (DTI) parameters and determine if Decorin could prevent these changes.

**Methods:** Communicating hydrocephalus was induced in 3-week-old rats with basal cistern injections of kaolin; age-matched controls were intact ( $n=4$ ) and kaolin-no treatment ( $n=4$ ) animals. Immediately following kaolin injections, animals received a 14-day continuous intraventricular infusion of phosphate-buffered saline ( $n=6$ ) or human recombinant Decorin ( $n=5$ ) via osmotic minipumps. At 14 days post-kaolin, all rats underwent MRI/DTI scanning followed immediately by sacrifice and brain fixation. DTI voxel-based analysis was performed on 4 serial rostral-to-caudal slices to quantify mean fractional anisotropy (FA), diffusivity (MD), axial diffusivity (AD) and radial diffusivity (RD) of the corpus callosum (CC) and periventricular white matter (PVWM). Immunohistochemistry and stereology were employed to quantify astrogliosis (GFAP) and aquaporin-4 (AQP4) levels in the CC and PVWM at caudal levels.

**Results:** Compared to intact animals (rostral  $1.3\pm 0.1$  and caudal  $0.9\pm 0.1$  ventricular volume), the caudal lateral ventricles were significantly larger in kaolin-only ( $16.2\pm 2.8$ ,  $p=0.005$ ) and kaolin-PBS ( $21.0\pm 5.4$ ,  $p<0.001$ ) animals than rostral portions ( $8.0\pm 1.7$  and  $10.1\pm 3.8$ , respectively). Following this gradient, untreated hydrocephalic rats exhibited significantly ( $p<0.01$ ) decreased FA and increased RD in the caudal-most CC and increased MD and AD in the caudal PVWM compared to intact controls. Decorin significantly ( $p<0.05$ ) reversed the RD and MD changes in the caudal CC and PVWM MD ( $p<0.05$ ). Such DTI reversals were not discovered in the rostral CC and PVWM. A significant increase in GFAP immunostaining resulted in a positive correlation ( $p<0.05$ ) between CC GFAP levels and the caudal-most CC RD. In the caudal PVWM, MD and AQP4 levels and AD and GFAP presence were positively correlated ( $p<0.01$ ).

**Conclusions:** These results indicate that regional differences exist in ventricular and DTI parameters, and that Decorin has the therapeutic potential to decrease microstructural damage in juvenile hydrocephalus.

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## O60

### Comparison of invasive ICP measurements to Distortion Product Otoacoustic Emissions (DPOAE) in adults during infusion testing for INPH

MA Williams<sup>1\*</sup>, SE Voss<sup>2</sup>, NJ Horton<sup>3</sup>, J Malm<sup>4</sup>, A Eklund<sup>4</sup>

<sup>1</sup>The Sandra and Malcolm Berman Brain & Spine Institute, USA; <sup>2</sup>Smith College, USA; <sup>3</sup>Amherst College, USA; <sup>4</sup>Umeå University, Sweden

E-mail: michwill@lifebridgehealth.org

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**Introduction:** Noninvasive ICP measurements are needed for astronauts at risk for the Visual Impairment/Intracranial Pressure (VIIP) syndrome. We evaluated distortion product otoacoustic emissions (DPOAE) for potential use to monitor ICP changes noninvasively.

**Methods:** Eight subjects, mean age  $68.5\pm 7.4$  years (range 58-79 years), undergoing lumbar CSF infusion testing (Liquor Celda, Umeå, Sweden) for hydrocephalus had DPOAE measurements made during ICP recording in the supine and upright positions, and during the infusion testing at 6 different ICP levels. DPOAE were measured with the HearID system (Mimosa Acoustics, Champaign, IL) at 13 log-spaced frequencies between 500 and 4000 Hz. DPOAE magnitudes within 6 dB of the noise floor, due in part to presbycusis, were not analyzed, resulting in 5 of 13 frequencies with results that could be analyzed. Changes in DPOAE magnitudes and angles from the upright position were analyzed for these 5 frequencies at 7 ICP levels. For the DPOAE magnitudes and angles at each ICP and frequency, a 95% confidence interval was calculated using a bootstrap method. A statistically significant difference is present when the confidence interval does not contain zero.

**Results:** In general, increasing ICP resulted in decreasing DPOAE magnitude and increasing DPOAE angle at all frequencies. DPOAE angles show statistically significant changes with ICP for all 5 frequencies, and the changes increase systematically with increasing ICP. Statistically significant changes in DPOAE magnitudes were also present, but for fewer frequencies and only at higher ICP levels.

**Conclusions:** This is the first study to measure change in DPOAE magnitude and angle as a function of ICP. Systematic trends are present for both magnitude and angle; however DPOAE angle appears more robust, consistent with a previous study of DPOAE in patients undergoing LP and CSF removal. DPOAE may be more reliable in younger subjects with better hearing than the subjects evaluated in this study. For future use of DPOAE as a noninvasive ICP modality, if knowledge of the magnitude of ICP change (in mm Hg or kPa) in relation to change in DPOAE magnitude or angle is required, then an initial calibration of DPOAE with invasive ICP monitoring will be necessary.

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## O61

### Endovascular treatment considerations in Idiopathic Intracranial Hypertension (IIH)

Heinke Pulhorn<sup>\*</sup>, Arun Chandran, Mani Puthuran, Hans Nahser, Catherine McMahon

The Walton Centre, UK

E-mail: heinke.pulhorn@thewaltoncentre.nhs.uk

Fluids and Barriers of the CNS 2015, 12(Suppl 1):O61

**Introduction:** Impaired cerebral venous sinus outflow leading to cerebral venous hypertension has been implicated as a potential final common pathway in the pathophysiology of idiopathic intracranial hypertension (IIH). The aim of this study is to assess the role of endovascular management strategies in the form of either primary venous sinus angioplasty or venous stenting for refractory IIH.

**Method:** Retrospective study of 37 consecutive patients with refractory IIH and imaging evidence of cerebral venous sinus outflow impairment. Primary venous angioplasty or secondary stenting were performed and clinical outcomes were documented on a standardised proforma.

**Results:** 20 out of the 37 cases showed positive pressure gradients and had endovascular management where there was variable reduction of the pressure gradient. 17 (of whom 12 had only sinus venoplasty and 5 had venoplasty followed by sinus stenting) out of 20 showed clinical improvement or resolution of symptoms. 3 patients were refractory to endovascular management and stabilised after ventriculo-peritoneal shunting.

**Conclusion:** The pathophysiology of IIH from venous hypertension secondary to venous outflow impairment is controversial. A selected group of patients with IIH and cerebral venous outflow impairment can benefit from endovascular treatment. In our experience 60% of patients showed clinical improvement with primary sinus venous angioplasty alone. This is a potential alternative to CSF shunting or primary stenting of venous sinus. After additional venous sinus stenting of refractory cases 85% of our patients in our cohort improved clinically.

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#### O62

##### Venous sinus stenting immediately reduces intracranial pressure in Idiopathic Intracranial Hypertension patients with venous sinus stenosis

Samir A Matloob<sup>1</sup>, Ahmed K Toma, Simon D Thompson, Chee L Gan, Edward W Dyson, Claudia Craven, Aswin Chari, Neekhil A Patel, Huan Wee Chan, Syed Shah, Patricia Haylock-Vize, Jinendra Ekanayake, Fergus Robertson, Lewis Thorne, Laurence D Watkins  
National Hospital for Neurology and Neurosurgery, UK  
E-mail: amir.matloob@me.com

*Fluids and Barriers of the CNS* 2015, **12**(Suppl 1):O62

**Introduction:** Idiopathic Intracranial Hypertension (IIH) is characterised by an increased intracranial pressure (ICP) in the absence of any central nervous system disease or structural abnormality, and normal CSF composition. Management becomes complicated once surgical intervention is required. Venous sinus stenosis has been suggested as a possible aetiology for IIH. Venous sinus stenting has emerged as a possible interventional option. Evidence for venous sinus stenting is based on elimination of the venous pressure gradient and clinical response. There have been no studies demonstrating the immediate effect of venous stenting on ICP.

**Methods:** Patients with a potential or already known diagnosis of IIH were investigated according to departmental protocol. ICP monitoring was performed for 24 hours. When high pressures were confirmed, CT venogram and catheter venography were performed to look for venous stenosis to demonstrate a pressure gradient. If positive, venous stenting would be performed and ICP monitoring would continue for a further 24 hours after deployment of the venous stent.

**Results:** Ten patients underwent venous sinus stenting with concomitant ICP monitoring. Nine out of ten patients displayed an immediate reduction in their ICP that was maintained at 24 hours. The average reduction in mean ICP and pulsatility was significant ( $p=0.003$ ). Six out of ten patients reported a symptomatic improvement within the first 2 weeks.

**Conclusion:** Venous sinus stenting results in an immediate reduction in ICP. This physiological response to venous stenting has not previously

been reported. Venous stenting could offer an alternative treatment option in correctly selected patients with IIH.

#### O63

##### Are B waves of intracranial pressure suppressed by general anesthesia?

Despina Afroditi Lalou, Joseph Donnelly, Marek Czosnyka, Eva Nabbarja, Matthew Garnett, John D Pickard, Zofia Helena Czosnyka<sup>\*</sup>  
Neurosurgery, University of Cambridge, UK  
E-mail: zc200@medschl.cam.ac.uk

*Fluids and Barriers of the CNS* 2015, **12**(Suppl 1):O63

**Objective:** Our previous study indicated that the magnitude of ICP slow vasogenic waves (also known as B waves), recorded during infusion study in hydrocephalic patients, was significantly suppressed when the study was performed under general anesthesia (GA). This was suggested to be secondary to decreased brain metabolism rate in patients under GA, as estimated by CSF production rate found lower than in conscious patients. Limitation of the previous study was that infusion test, limited in time (average 30 minutes), is not ideal for the detection of power of slow waves (up to 3 minutes in duration) using traditional spectral analysis. We continued research in this direction, comparing overnight ICP monitoring in hydrocephalus (conscious patients) with patients after TBI without intracranial hypertension (monitored under GA).

**Methods:** Two groups of patients were studied: 30 with overnight ICP monitoring diagnosed for hydrocephalus and 30 consecutive TBI patients, without intracranial hypertension (confirmed by mean ICP < 18 mm Hg). The TBI patients were anesthetized and ventilated, with data recorded during first night of monitoring.

Mean ICP, pulse amplitude of ICP, magnitude of slow vasogenic waves (periods from 20 seconds to 3 minutes), and index of compensatory reserve RAP were compared using Mann-Whitney U test.

**Results:** Overnight magnitude of slow waves was greater in conscious patients than in patients under GA (1.5+/-0.43 versus 0.7+/- 0.41 mm Hg;  $p<0.5*10^{-7}$ ). Compensatory index RAP was slightly lower (although insignificantly) in GA than in conscious patients (0.31+/-0.17 vs 0.4+/-0.18;  $p=0.066$ ) indicating better compensatory reserve under GA. Pulse amplitude (peak to peak) was almost identical in two groups (5.7+/-4.1 mm Hg) and respiratory wave was greater in GA (ventilated) than in conscious patients (breathing spontaneously). Mean ICP was greater in GA than in conscious patients (13.8+/-2.9 vs 7.7+/-4.8 mm Hg;  $p=1*10^{-6}$ ).

**Conclusion:** Results confirm previous observations that under GA magnitude of slow ICP waves tends to be lower than in conscious patients. This was observed in parallel with better compensatory reserve under GA, probably due to the fact that anesthetised patients had lower PaCO<sub>2</sub> leading to a vasoconstriction. These differences should be taken into account in any methodology using the magnitude of slow ICP waves as a clinical biomarker.

#### O64

##### Relationship between CSF dynamics and outcome after shunting in NPH- 20 years of single centre experience

Eva Nabbarja, Marek Czosnyka, Nicole Keong, Matthew Garnett, John D Pickard, Zofia Helena Czosnyka<sup>\*</sup>  
Neurosurgery, University of Cambridge, UK  
E-mail: zc200@medschl.cam.ac.uk

*Fluids and Barriers of the CNS* 2015, **12**(Suppl 1):O64

**Objective:** The strict relationship between shunt-responsiveness and increased resistance to CSF outflow (Rout) as reported in 1981 by Borgensen and Gjerris [1] was later presented as significant but not strong in the 'Dutch NPH' trial [2] and recently reported as unconvincing in the 'European NPH study' [3]. We reviewed our ongoing database to study the relationship between parameters describing CSF circulation and pressure-volume compensation with clinical improvement after shunting.

**Method:** 310 adult patients (age 40-86) were included in retrospective analysis. All patients had probable NPH following clinical assessment including imaging. Patients underwent lumbar or intraventricular infusion studies and were available for follow-up via the multidisciplinary CSF clinic. Outcomes were assessed using the in-house Cambridge Outcome Scale; a pragmatic categorization of patient cohorts into three groupings – sustained



improvement, short-term improvement and no improvement. Compensatory parameters were calculated on the basis of infusion test: baseline ICP and pulse amplitude, Rout, elasticity, estimator of CSF production, slope of amplitude-pressure regression line. Consultants deciding about shunting were not blind to results of infusion study.

**Results:** 79% of patients showed improvement (60% sustainable, 19% temporary). Improvement rate increased from 1992 (60%) to 2013 (86%);  $p=0.0003$ . Of all calculated CSF compensatory parameters, only Rout was associated with outcome ( $p=0.014$ ). Pulse amplitude of ICP (peak-to-peak), slope of amplitude-pressure regression line, elasticity, did not correlate with outcome significantly. Patients with  $Rout > 13$  mm Hg/(ml/min) had an improvement rate of 79%, compared to 63% ( $p=0.011$ ) with  $Rout < 13$ . Notably, none of patients with low Rout (lower than 6 mm Hg/(ml/min);  $N=5$ ) improved after shunting. Neither age nor sex correlated with outcome.

**Conclusion:** Rout was the only CSF compensatory parameter correlating with outcome following shunting. The relationship was weak but significant. Infusion studies appeared to be helpful in the assessment of compensatory parameters both for diagnostic and to yield baseline values as a benchmark for further investigations in cases of suspected shunt malfunctions and complications.

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#### O65

##### Intracranial pressure and venous sinus pressure gradients: what happens 3 months after stenting?

Hasan Asif, Claudia Craven<sup>1</sup>, Syed N Shah, Simon D Thompson, Aswin Chari, Samir A Matloob, Neekhil A Patel, Edward W Dyson, Patricia Haylock-Vize, Andrew R Stevens, Huan Wee Chan, Jinendra Ekanayake, Tarek Mostafa, Ahmed K Toma, Laurence D Watkins  
Victor Horsley Department of Neurosurgery, National Hospital for Neurology & Neurosurgery, Queen Square, London, UK  
E-mail: claudia.craven@gmail.com

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**Introduction:** Benign Intracranial hypertension (BIH) is commonly associated with venous sinus stenosis. Increasingly, this is treated endovascularly with stent insertion. However, this treatment modality is still controversial. Clinical improvement post stent insertion has been described. Little is known about long-term control of intracranial pressure (ICP). In our unit, catheter cerebral venogram with pressure measurements is routinely performed 3 months post stent insertion in BIH patients. We aim to quantify the degree of venous pressure changes in stenosis patients treated with sinus stenting and how the changes correlate with radiographic improvements.

**Methods:** Single Centre case series. Clinical, angiographic and intracranial pressure data before and 3 months after stent placement were reviewed. All venograms were done under local anesthetic in supine position.

**Results:** Between 2011 and 2015, 33 patients underwent post stent insertion cerebral venogram as a routine follow up. Mean pre-stent superior sagittal sinus pressure was  $28.8 \pm 2.0$  mmHg (mean $\pm$ SEM). Mean 3-months post-stenting superior sagittal sinus pressure was  $10.5 \pm 0.7$  mmHg ( $p < 0.0001$ ). Pre-stenting pressure gradients across stenosis were reduced from  $18.3 \pm 11.9$  mmHg to  $6.3 \pm 4.5$  mmHg 3-months post-stenting ( $p < 0.0001$ ). 25 of the 33 patients showed radiological stent patency and stenosis obliteration. Five developed new focal narrowing distal and three proximal to the stent.

**Conclusions:** This study provides objective evidence of the effectiveness of venous sinus stent insertion in reducing intracranial pressure 3 months post procedure in the majority of patients with intracranial hypertension and focal venous sinus stenosis. Angiographic evidence of patent sinuses correlated with reduction in pressure gradients.

#### O66

##### Integration of CSF pressure and flow data to further investigate nature of cerebrospinal compliance in hydrocephalus

Simon Garnotel<sup>1\*</sup>, Eric Schmidt<sup>2</sup>, Zofi Czosnyka<sup>3</sup>, Marc Baroncini<sup>4</sup>, Gwenaël Pagé<sup>1</sup>, Olivier Balédent<sup>1</sup>

<sup>1</sup>University of Picardie Jules Verne, BioFlow Image Laboratory, Amiens, France; <sup>2</sup>University hospital of Toulouse, Neurosciences Department, Toulouse, France; <sup>3</sup>University of Cambridge, Department of Clinical Neurosciences, Cambridge, UK; <sup>4</sup>University hospital of Lille, INSERM U837, Jean-Pierre AUBert Research Center, Lille, France  
E-mail: simon.garnotel@u-picardie.fr

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**Introduction:** Intracranial pressure (ICP) monitoring and infusion test are widely used in the diagnosis and management of hydrocephalus. MR neuroimaging allows the quantification of cerebrospinal fluid (CSF) and blood flow dynamics that can be used to calculate intracranial volume changes (IVC) during cardiac cycle and to help diagnose active hydrocephalus which need the placement of a shunt. Since compliance is a function of ICP and IVC changes, the aim of this work is to combine these two techniques to calculate the cerebrospinal system compliance along the cardiac cycle.

**Methods:** 36 patients with suspected hydrocephalus underwent a spinal infusion test: a constant rate infusion of 1 mL/min was administered until pressure reached a specific threshold. Pressure sensor data was recorded with ICM+. Previously all patients had a morphological MRI, in which two PC-MRI measurements were performed to quantify the dynamics of CSF and cerebral arterial and venous flows, which move through the cranium during the cardiac cycle. These flows have been extracted by the homemade software Flow Analysis.

A homemade "ICP/flow analysis" software was developed to calculate the mean ICP cycle over the cardiac cycle in four periods of the infusion procedure (basal, up, plateau, down) from ICM+ extracted data. It calculates the IVC curve during the cardiac cycle, which generates ICP changes, from Flow Analysis extracted data and determines the compliance change of the cerebrospinal system during cardiac cycle, function of the previous mean ICP and IVC results.

**Results:** The ICP/flow analysis software was used on the 36 patients, in whom the final clinical diagnosis was still unknown. For the different periods of the infusion test, the amplitudes of ICP were:  $12 \pm 3$  mmHg for basal,  $24 \pm 4$  for up,  $32 \pm 6$  for plateau,  $24 \pm 5$  for decrease of ICP after infusion. From flow MRI, IVC was equal to  $683 \pm 341$  mm<sup>3</sup>. The mean values of the compliance in the cardiac cycle over all the patients were equal to  $476 \pm 292$  and  $120 \pm 110$  mm<sup>3</sup>/mmHg during the basal and the plateau period, respectively. These results show significant compliance variability over the cardiac cycle, especially a decrease in its value in the middle of the cycle, when volume and pressure are increased. An exponential correlation was found between the mean value of compliance and ICP amplitude during basal and plateau periods with a correlation coefficient of 0.85.

**Conclusions:** A multi-platform ICP/flow analysis software was performed to combine ICP, CSF and cerebral blood flow changes during a short time of a cardiac cycle. These results create a new point of view on the cerebrospinal system compliance, showing that it is not constant during the cardiac cycle and that significant variability exists in patients suffering from NPH.

#### O67

##### Intracerebral pressure waves and sleep disordered breathing

Aruna S Rao<sup>1\*</sup>, David Solomon, Abhay R Moghekar  
The Johns Hopkins Hospital, USA  
E-mail: arao10@JHMI.edu

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**Introduction:** Increases in Intracerebral pressure (ICP) have been reported to occur in patients with sleep disordered breathing (SDB) in association with the periods of oxygen desaturation. These studies however, involved very small sample sizes.

**Objective:** The purpose of our study was to assess the relationship between alterations in ICP and oxygen desaturations using a large cohort

of patients undergoing continuous Spinal fluid pressure monitoring for evaluation of hydrocephalus.

**Methods:** Patients admitted to the CSF disorders unit for continuous spinal fluid pressure monitoring were selected for analysis. The pressure waves were recorded via pressure transducer attached to an indwelling Codman spinal catheter. Oxygen saturation was recorded by pulse oximetry. The Spinal fluid pressure waves and oxygen saturation waveforms were converted to digital format for analysis. Our outcome variables were 1. Oxygen desaturation defined as 4% below or 96% of the mean 2. Elevated ICP defined as values above the median value for each patient.

We dichotomized the Oxygen data into normal or desaturations and ICP data to above or below the median ICP. We computed the association between Dichotomized Oxygen saturation versus dichotomized ICP using the chi square test. We analyzed desaturations with ICP as a continuous variable using the t test.

**Results:** A consecutive series of 100 patients (median age was 61.5 years; 58% were women) were analyzed. We found that oxygen saturation was more likely to be low immediately after an instance of elevated ICP and ICP is significantly higher immediately before periods of oxygen desaturation. This finding was statistically significant association ( $p < 0.05$ ) in 39 (39%) of patients. A diagnosis of NPH did not differ between the 2 groups ( $p=0.2$ ) but a confirmed diagnosis of SDB did ( $p=0.07$ ).

**Conclusion:** In patients with continuous spinal fluid pressure monitoring, small but consistent elevations in spinal fluid pressure are associated with oxygen desaturations in patients with sleep disordered breathing.

## POSTER PRESENTATIONS

### P1

#### Real time US –guided ventricular catheterisation: a single centre retrospective audit

Erjon Agushi\*, James Montgomery Barber, Konstantina Karabatsou  
Salford Royal NHS Foundation Trust, UK  
E-mail: erjon.agushi@srft.nhs.uk

*Fluids and Barriers of the CNS 2015, 12(Suppl 1):P1*

**Introduction:** Suboptimal shunt or external ventricular device (EVD) catheter placement can result in significant morbidity, requiring system revision and consequently prolonging in-hospital stay. Multiple incorrect trajectories can potentially cause further complications and neurological deficits. While experienced operators can achieve relatively high success rates with the craniometric technique, the failure rates can be even greater than 20%, in certain studies.

**Design:** Retrospective audit of documented method of guidance technique and subsequent clinical/radiological outcomes.

**Objective:** The objective of our study was to compare the clinical benefits of real-time Ultrasound guidance in enhancing ventricular catheter insertion versus the standard craniometric-guided free-hand technique.

**Methods:** Operative records, clinical outcomes and postoperative scans of the patients who underwent EVD or shunt insertion from between March 2013 to March 2014 at a single centre were reviewed retrospectively.

**Results:** A total of 162 patients' clinical notes and scans were reviewed. 22 were excluded due to unclear documentation, missing operative notes or postoperative scan having not been performed. 78 underwent an EVD insertion, mainly for secondary hydrocephalus due to SAH, whereas 62 had insertion of a VP shunt as a primary procedure. Use of US to visualize the ventricles was documented in 57.9% (56.4% in EVDs vs. 59.7% in shunts), while usage of real-time US guidance of catheter insertion was recorded in 42.1% (39.7% in EVDs vs. 45.2% in shunts). Incorrect or suboptimal positioning was significantly higher in the free-hand cohort as compared to the US guided group (22.3% vs. 5.1% respectively,  $p=0.005$ ). Only one shunt was revised due to dysfunction in the real-time US guided group vs. 3 shunts and 5 EVDs in the free-hand group (1.7% vs. 10%,  $p=0.049$ ). Postoperative focal deficits were only recorded being present in patients undergoing free-hand insertion.

**Conclusions:** Insertion of ventricular catheters under US guidance enables safe and optimal catheter placement, reducing significantly the rate of revisions and subsequent morbidity.

### P2

#### The relationship between patient height and intracranial pressure in children and adults

Trine Hjorslev Andreassen\*, Sarah Skovlunde Hornshøj, Alexander Lilja, Morten Andresen, Marianne Juhler  
Copenhagen University Hospital Rigshospitalet, Denmark  
E-mail: trinehjorslev@hotmail.com

*Fluids and Barriers of the CNS 2015, 12(Suppl 1):P2*

**Introduction:** The management of increased intracranial pressure (ICP) and monitoring of ICP is an important part of neurosurgery, but reference values for ICP have not been established differentiating between children and adults. The same estimated reference of 7-15 is used indiscriminately for children and adults, and does not take in to account that adults and children differ physiologically. The effect on ICP of a postural change from a supine to a upright standing position has been established, though the association between height and ICP in upright position has not been studied. The purpose of this study is to address if ICP values could depend on height.

**Methods:** Patients having a shunt were excluded from the study in order to avoid the influence of mechanical siphoning. Forty-one patients undergoing diagnostic ICP monitoring for a suspicion of hydrocephalus or idiopathic intracranial hypertension (IIH) were included in this study. Data were consecutively and prospectively collected. Nine were children (age 7-17) and thirty-two were adults (age 23-85). ICP was measured in parenchyma by either a cable-based or a telemetric probe. Measurements included both a supine and a upright standing position, and changes in ICP were calculated.

**Results:** Mean height was 152.3 cm (range 122-180) for children and 169.4 cm (range 155-188) for adults. Height did not appear to have an impact on measured ICP in either supine ( $p = 0.15$ ) or upright standing position ( $p = 0.28$ ). Changing body position from supine to upright caused a significant decrease in ICP in both children (median decrease 9.8 mmHg;  $p = 0.008$ ) and adults median decrease 12.5 mmHg;  $p < 0.001$ ).

In the entire group there was borderline significance between patient height and the calculated postural decrease in ICP occurring when the patient changed from a supine to a upright standing position ( $p = 0.053$ ). When dividing into children and adults, the change in ICP correlated to height was significant in children ( $p = 0.022$ ), but not in adults ( $p = 0.34$ ).

**Conclusions:** We did not establish a direct correlation between ICP and height. However, in children we found a relationship between height and ICP decrease going from supine to upright. A similar correlation was not found in adults. Our results may be important for approaches to physiological risks of overdrainage caused by shunting.

### P3

#### Cavum septum pellucidum: a novel endoscopic approach to the posterior third ventricle

Hasan Asif\*, Nithish Jayakumar, Peter Heppner  
Department of Neurosurgery, Starship Children's Hospital, Auckland, New Zealand  
E-mail: hasan.asif09@imperial.ac.uk

*Fluids and Barriers of the CNS 2015, 12(Suppl 1):P3*

**Objectives:** To describe a novel endoscopic approach to the posterior third ventricle through a cavum septum pellucidum.

**Design and subjects:** Retrospective case review of a 7-year old boy with a tectal plate mass.

**Methods:** The clinical and operative notes, operative videos, and imaging were reviewed. A literature search was also performed.

**Results:** The patient was referred for neurosurgical opinion due to a 2-week history of gait instability on a background of progressive ataxia and urinary incontinence. MRI showed triventricular hydrocephalus due to a tectal plate mass with thalamic extension.

On examination, his GCS was 15/15 and he demonstrated truncal ataxia, gait instability, and upper limb dysmetria. He was admitted for an endoscopic third ventriculostomy with biopsy.

**Operative approach:** The patient was anaesthetised and placed supine. Incision and burr hole were over the left coronal suture. A third ventriculostomy was performed for hydrocephalus.

The tumour was then approached through the cavum septum pellucidum. Septal fenestrations allowed easy access to the cavum. Internal cerebral

veins were identified and the velum interpositum opened with sharp scissors. The opening was dilated and an endoscope advanced into the posterior third ventricle. The tumour was identified and biopsies obtained. He had a satisfactory recovery and was discharged 6 days later. Histology showed a low-grade glioma, which remained stable on follow-up MRI. **Conclusions:** When present, the cavum septum pellucidum provides a viable alternative route to the posterior third ventricle.

#### P4

##### Longitudinal clinical observation of 4 patients with preclinical stage of idiopathic normal pressure hydrocephalus

Shingo Azuma<sup>\*</sup>, Takashi Suehiro, Hiroaki Kazui, Shunsuke Sato, Yukiko Suzuki, Hideki Kanemoto, Kenji Yoshiyama

Osaka University Graduate School of Medicine, Japan

E-mail: shingo.azuma.328@gmail.com

Fluids and Barriers of the CNS 2015, 12(Suppl 1):P4

**Introduction:** In patients with idiopathic normal pressure hydrocephalus (iNPH) with features of Disproportionately Enlarged Subarachnoid-space Hydrocephalus (DESH), ventriculomegaly and the tight high-convexity and medial subarachnoid spaces appear in magnetic resonance (MR) images before the occurrence of objective symptoms. There are few reports of longitudinal observation of clinical course in DESH-type iNPH patients with no objective symptom.

**Methods:** We longitudinally observed 4 patients (1 female and 3 males with a mean age of 73.8 years) with features of DESH who visited the neuropsychological clinic in our hospital, whose symptoms were not apparent in the first visit. We evaluated the triad symptoms with iNPHGS and conducted the cognitive and gait examinations once a year. We also evaluated quantitative rCBF of those patients by 123I-IMP single photon emission computed tomography (SPECT) using the autoradiography (ARG) method.

**Results:** Based on the scores of iNPHGS, we classified 4 patients into two groups; two stable patients and two deteriorated patients. In one patient of the stable group, the score of the Mini-mental State Examination (MMSE) did not change and the score of the Frontal Assessment Battery (FAB) and the Timed Up & Go Test (TUG) improved, however, in the other patient, the score of MMSE, FAB and TUG worsened. In the deteriorated group, one patient expressed the gait disturbance and the other patient did the gate disturbance and the cognitive impairment. In the former patient, the score of MMSE and FAB worsened and a wide-based gait and the disturbance of the dynamic equilibrium appeared, although the score of TUG did not change. In the latter patient, the score of FAB and TUG worsened but the score of MMSE did not change. The changes of quantitative rCBF of 4 patients were various.

**Conclusions:** The different clinical courses and changes of quantitative rCBF were observed in each patient.

#### P5

##### Amyloid deposition and ApoE4 carriers in idiopathic normal pressure hydrocephalus

Masahiko Bundo<sup>\*</sup>, Akinori Nakamura, Takashi Kato, Shunpei Niida, Kaori Iwata, Chihomi Sawado, Kengo Ito

National center for geriatrics and gerontology, Japan

E-mail: ibundou@ncgg.go.jp

Fluids and Barriers of the CNS 2015, 12(Suppl 1):P5

**Introduction:** It is known that idiopathic normal pressure hydrocephalus (iNPH) can co-morbid with Alzheimer disease (AD). Previous studies, probing amyloid (A $\beta$ ) deposition by cortical biopsy during a ventriculo-peritoneal shunt, have shown that A $\beta$  deposition was found in 40–45 % of iNPH patients. However, the reason for this high prevalence is not well understood. Therefore, the objective of this study was to investigate whether the prevalence of the A $\beta$  deposition in iNPH is explainable by a simple overlap of the AD pathology in general population, or is modified by some specific effects of iNPH.

**Methods:** In this study, 11C-Pittsburgh compound B (11C-PiB) PET and Apolipoprotein E genotype were examined in age- matched 70 Cognitively Normal Elderly (CNE), 19 Alzheimer disease (AD) and 31 probable iNPH patients, to investigate the risk of co-morbidity of AD in

iNPH patients. The chi-square analysis was used for the statistical analysis. The Bonferroni correction was used for the multiple comparisons.

**Results:** Amyloid deposition was shown in 19.0% of CNE, 81.3% of AD, and 52.0% of iNPH, while ApoE4 carriers were found in 19.0% of CNE, 73.7% of AD, and 29.0 of iNPH. The rate of amyloid deposition of iNPH was significantly higher than CNE ( $p < 0.005$ ) and lower than AD ( $p < 0.005$ ). On the other hand, the probability of the apoE4 carriers in iNPH was significantly lower than AD ( $p < 0.005$ ), but did not show any significant difference from CNE ( $p = 0.56$ ).

**Conclusions:** In iNPH, the rate of amyloid deposition is higher than CNE, while there were no differences in the probability of the ApoE4 carriers. These results suggest that iNPH patients may have some mechanisms to facilitate the amyloid deposition.

#### P6

##### Non-invasive assessment of ICP during infusion test using Transcranial Doppler Ultrasonography

Danilo Cardim<sup>1</sup>, Brenno Cabella<sup>1</sup>, Joseph Donnelly<sup>1</sup>, Chiara Robba<sup>2</sup>, Marek Czosnyka<sup>1</sup>, Matthew Garnett<sup>1</sup>, John D Pickard<sup>1</sup>, Zofia Helena Czosnyka<sup>1\*</sup>

<sup>1</sup>Neurosurgery, University of Cambridge, UK; <sup>2</sup>Dept of Anesthesiology,

University of Genoa, Italy

E-mail: zc200@medschl.cam.ac.uk

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**Background:** Transcranial Doppler (TCD) based methods have been used to estimate ICP noninvasively (nICP), however their relative accuracy varies between different types of intracranial hypertension: vasogenic, CSF circulatory or secondary to brain volumetric changes (oedema, contusion, hematoma, etc). This study aimed to compare four nICP methods in a prospective cohort of hydrocephalus patients whose CSF dynamics was investigated using infusion tests involving controllable test-rise of ICP.

**Methods:** FV, ICP and non-invasive ABP were recorded in 53 patients diagnosed for hydrocephalus. nICP methods were based on: I) interaction between FV and ABP using black-box model (nICP\_BB); II) diastolic FV (nICP\_FVd); III) critical closing pressure (nICP\_CrCP) and IV) TCD-derived pulsatility index (nICP\_PI). Correlation between rise in ICP ( $\Delta$ ICP) and  $\Delta$ nICP and averaged correlations for changes in time between ICP and nICP during infusion test were investigated.

**Results:** All nICP formulas overestimated ICP at baseline ( $p < 0.005$ ): nICP\_BB 10.76 (15.08-7.30); nICP\_FVd 16.97 (22.56- 11.64); nICP\_CrCP 18.34 (20.38-14.89); nICP\_PI 16.57 (17.46-16.06). At plateau of ICP during infusion test, only nICP\_BB and nICP\_PI presented significant difference from ICP. From baseline to plateau, all nICPs estimators increased significantly (paired t-test,  $p < 0.05$ ). Correlations between  $\Delta$ ICP and  $\Delta$ nICP were better represented by ICPn\_PI and ICPn\_BB: 0.45 and 0.30 ( $p < 0.05$ ). nICP\_FVd and nICP\_CrCP presented non-significant correlations: -0.17 ( $p = 0.21$ ), 0.21 ( $p = 0.13$ ). For changes in ICP during individual infusion test ICPn\_PI, ICPn\_BB and ICPn\_FVd presented similar correlations with ICP:  $0.39 \pm 0.40$ ,  $0.39 \pm 0.43$  and  $0.35 \pm 0.41$  respectively. ICPn\_CrCP presented a weaker correlation ( $R = 0.29 \pm 0.24$ ). In those cases where changes of ICP related to vasogenic fluctuations (plateau waves, B waves) overlapped rise related to CSF infusion, time- correlation between real and estimated ICP seemed to be remarkably better.

**Conclusions:** Out of the 4 methods, nICP\_PI was the one with best performance for predicting changes in  $\Delta$ ICP during infusion test, followed by nICP\_BB. nICP\_FVd and nICP\_CrCP showed unreliable correlations. Changes of ICP observed during the test were expressed by nICP values with only a moderate correlations. Vasogenic components of ICP seemed to be easier to estimate with TCD, than component related to increased CSF circulation.

#### P7

##### Cerebrospinal fluid biomarkers in patients with idiopathic normal pressure hydrocephalus with temporary response to shunt insertion

Huan Wee Chan<sup>\*</sup>, Patricia Anne Haylock-Vize, Edward William Dyson, Aswin Chari, Claudia Craven, Samir A Matloob, Neekhil A Patel, Simon D Thompson, Syed N Shah, Andrew R Stevens, Jinendra Ekanayake, Ahmed K Toma, Laurence Dale Watkins

The National Hospital for Neurology and Neurosurgery, UK

E-mail: chanhuanwee@gmail.com

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**Introduction:** Obstruction to cerebrospinal fluid (CSF) flow in idiopathic normal pressure hydrocephalus (iNPH) results in reduced CSF total tau (t-tau) and amyloid- $\beta$  42 (A $\beta$ 42) protein concentrations [1]. Restoration of normal CSF flow dynamics with ventriculoperitoneal (VP) shunt allows these biomarkers to clear from extracellular fluid into the CSF(1). CSF biomarkers in iNPH have been an interesting subject with initial results suggestive of reduced t-tau and amyloid- $\beta$ . A subgroup of probable iNPH patients responds favorably to VP shunt insertion but for a brief period (temporary responders). In our unit, these patients are further investigated with assessment of the effect of shunt tapping on walking speed. A large proportion underwent shunt revision. In this population, CSF biomarkers were studied over a prolonged period of time.

**Methods:** We included 5 patients (4 females; 1 male; mean age 77 years; age range 68-94 years) with temporary shunt responsive iNPH in the study. CSF t-tau and A $\beta$ 42 protein levels were measured at the time of lumbar drainage prior to initial shunt insertion, during shunt insertion, shunt tap to investigate shunt function and finally at shunt revision. The changes in these biomarkers were calculated.

**Results:** The duration between the first sample and the last sample at shunt revision was  $527.8 \pm 99.7$  days (mean $\pm$ SD). The mean t-tau levels were 181.7pg/ml, 821.0pg/ml, 392.5pg/ml and 492.25pg/ml at the time of lumbar drainage, during first shunt insertion, shunt tap and during shunt revision, respectively. The corresponding mean A $\beta$ 42 levels were 465.0pg/ml, 407.8pg/ml, 646.75pg/ml and 472.25pg/ml, respectively.

**Conclusions:** Our results demonstrated features suggestive of mild degenerative pathology distinct from Alzheimer's pattern. It remains to be proven if CSF drainage alters the biomarkers levels.

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#### P8

##### Does a temporizing measure of cerebrospinal fluid drainage as the initial procedure alter the surgical outcome in premature infants with post-hemorrhagic hydrocephalus?

Eisha Anne Christian<sup>1</sup>, Edward Melamed<sup>2</sup>, Edwin Peck<sup>1</sup>, Mark D Krieger<sup>1,2</sup>, J Gordon McComb<sup>1,2</sup>

<sup>1</sup>University of Southern California, Los Angeles, CA, USA; <sup>2</sup>Children's Hospital Los Angeles, CA, USA

E-mail: echristi@usc.edu

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**Objective:** It has been speculated whether the insertion of a temporary device to control hydrocephalus secondary to intraventricular hemorrhage (IVH) in the preterm neonate with removal of the debris caused by such a hemorrhage, can reduce subsequent complications following insertion of a permanent cerebrospinal fluid (CSF) diverting shunt. This retrospective review is directed at examining this speculation.

**Methods:** A retrospective review of the medical records of all premature infants surgically treated for post-hemorrhagic hydrocephalus (PHH) between 1997 and 2012 at our institution was undertaken.

**Results:** Over 14 years, 91 preterm infants with PHH were identified. The initial procedure for 50 neonates was the insertion of a ventricular reservoir (VR) that was serially tapped for varying time periods. For the remaining 41 premature infants, a ventriculoperitoneal/atrial shunt (VS) was the first procedure. Patients with a VR as their initial procedure underwent CSF diversion significantly earlier in life than those who had VS as the initial procedure (29 vs. 56 days,  $p < 0.01$ ). Of the infants with a VR as their initial procedure, 5/50 (10%) did not undergo a subsequent VS. The number of shunt revisions and the rates of loculated hydrocephalus and shunt infection did not statistically differ between the two groups.

**Conclusion:** Patients with initial VR insertion received a CSF diversion procedure at a significantly younger age than those who received a permanent shunt as their initial procedure. Otherwise, the outcomes with regards to shunt revisions, loculated hydrocephalus, and shunt infection were not different for the two groups.

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#### P9

##### Differential compartment overdrainage syndrome

Claudia Craven<sup>1</sup>, Neekhil A Patel, Samir A Matloob, Edward W Dyson, Aswin Chari, Tarek Mostafa, Simon D Thompson, Patricia Haylock-Vize, Syed N Shah, Andrew R Stevens, Huan Wee Chan, Jinendra Ekanayake, Ahmed K Toma, Laurence D Watkins

Victor Horsley Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, Queen Square, London, UK

E-mail: claudia.craven@gmail.com

*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:P9

**Introduction:** We describe a consistently similar clinical presentation of patients with complex hydrocephalus and encysted fourth ventricle separately drained by infratentorial shunt insertion.

**Methods:** A retrospective single centre case series. Medical notes were reviewed for clinical presentation, brain imaging and neurophysiological tests results. All patients underwent ICP monitoring using Spiegelberg bolt. Outcomes were determined by retrospective analysis of 24-hour ICP monitoring results, ventricular appearance on brain imaging CT and symptomatic improvements post-operatively.

**Results:** Five adult patients were referred to the hydrocephalus service in our unit with separate infra and supratentorial shunt systems. Clinical presentation included: bilateral lower motor neuron facial palsy, ophthalmoplegia, dysphonia, impaired gait headache and nausea. No patient experienced deafness. Two subjects had their facial nerve palsy confirmed with electrophysiology studies. Brain stem evoked potentials also confirmed sparing of the 8th cranial nerve. 24 hours ICP monitoring confirmed clear low pressures.

These patients underwent shunt revision connecting the supra and infratentorial shunt systems to achieve equal pressure drainage, with subsequent addition of a distal valve. Further ICP monitoring confirmed normalisation of pressure. All patients reported improvement in headaches and nausea, with a mild improvement in gait and dysphagia. On the other hand, facial weakness and ophthalmoplegia were persistent. All subjects had improved ventricular appearance on CT scans post revision. In the follow up period of 3 months no patient required further shunt revision.

**Conclusion:** Supra and infratentorial shunt construct in adults with encysted fourth ventricles should be similar to the shunt system widely known in the paediatric population with Dandy Walker syndrome, i.e. joint output to a single valve distal to the connection of the 2 drainage proximal catheters.

#### P10

##### Shunt assistant device deception due to pseudovertical posturing

Claudia Craven<sup>1</sup>, Neekhil A Patel, Hasan Asif, Aswin Chari, Edward W Dyson, Samir A Matloob, Patricia Haylock-Vize, Simon D Thompson, Syed N Shah, Andrew R Stevens, Tarek Mostafa, Huan Wee Chan, Jinendra Ekanayake, Ahmed K Toma, Laurence D Watkins

Victor Horsley Department of Neurosurgery, National Hospital for Neurology & Neurosurgery, Queen Square, London, UK

E-mail: claudia.craven@gmail.com

*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:P10

**Introduction:** The ever present need to balance over drainage with under drainage in hydrocephalus has required innovations including adjustable valves with antigravity devices. These are activated in the vertical position to prevent siphoning. We describe a group of patients who presented with unexplained under drainage caused by activation of antigravity shunt components produced by peculiar head/body position.

**Methods:** Single centre case series of hydrocephalus patients, treated with ventriculo-peritoneal shunt insertion. These patients presented with clinical and radiological under drainage syndrome. Medical notes were reviewed for clinical picture and outcome. Radiological studies were reviewed assessing shunt placement and ventricular size.

**Results:** Four patients presented with clinical and radiological under drainage syndrome. A consistent posturing of long term hyper-flexion of the neck whilst lying supine was observed. All patients had similar shunt construct (adjustable Miethke proGAV valve and shunt assistant antigravity component). In each of those patients a hypothesis was formulated that neck flexion was activating the shunt assistance antigravity component in supine position. All patients underwent shunt revision surgery removing the shunt assistant device from the cranium and adding an antigravity component to the shunt system at the chest. All patients had clinical and radiological improvement.

**Conclusions:** The combination of raised ICP when supine and a resistant shunt assistant could be blamed for worsening hydrocephalus. In bedridden hydrocephalus patients with a shunt assistant, consider the possibility of shunt deception due to abnormal neck positioning. In these patients, antigravity devices should be placed at the chest.

## P11

### Persistent CSF leak post spinal surgery and cerebrospinal fluid dynamic disturbances: cause or consequence?

Claudia Craven<sup>1</sup>, Neekhil A Patel, Akbar A Khan, Simon D Thompson, Edward W Dyson, Samir A Matloob, Aswin Chari, Patricia Haylock-Vize, Syed N Shah, Andrew R Stevens, Tarek Mostafa, Huan Wee Chan, Jinendra Ekanayake, Ahmed K Toma, Laurence D Watkins  
Victor Horsley Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, Queen Square, London, UK  
E-mail: claudia.craven@gmail.com

Fluids and Barriers of the CNS 2015, 12(Suppl 1):P11

**Introduction:** Cerebrospinal fluid (CSF) leak following spinal surgery is a relatively common surgical complication. A small group of CSF leak patients require multiple surgical repairs and prolonged hospital admission. Spinal CSF leaks are usually classically associated with symptoms of low intracranial pressure (ICP). However, there is a paucity of literature investigating the associated CSF dynamics.

**Methods:** Retrospective case series study of patients with persistent CSF leak referred to the hydrocephalus service in our unit for intracranial pressure monitoring. Medical notes were reviewed for clinical presentation, management and outcome. Images were reviewed and ICP data were analysed. All patients underwent Continuous ICP monitoring using Spiegelberg ICP bolts.

**Results:** 3 Patients had cervical, thoracic and lumbosacral complex spinal fixation surgery, complicated by prolonged CSF leaks (mean of 56 days from day of surgery to resolution). Each patient required 2 re-explorations spinal surgeries and multiple lumbar drains insertions prior to 24 hours ICP monitoring. Two patients were shown to have mildly raised ICP (>15.2mmHg) and all three had abnormal pulse amplitudes (>5mmHg). One patient underwent catheter cerebral venogram that demonstrated focal stenosis of the distal right transverse sinus with a significant pressure gradient. This patient underwent a right transverse venous sinus stent insertion. This resulted in resolution of headaches, prevention of impending wound breakdown and normalisation of ICP data. Two patients underwent insertion of ventriculo-peritoneal shunts (VPS). Both had resolution of their CSF leaks immediately post VPS insertion and were discharged from hospital.

**Conclusion:** Our results suggest that abnormal cerebrospinal fluid dynamics should be explored in patients with persistent CSF leak post spinal surgery. Whether abnormal pressure and dynamics represent a pre-existing abnormality or is induced by spinal surgery should be subject for further studies.

**Abbreviations:** ICP: Intra Cranial Pressure; VPS: Ventriculo-peritoneal shunt.

## P12

### Learning to control ICP

Jinendra Ekanayake<sup>1</sup>, Aswin Chari, Claudia Craven, Simon D Thompson, Syed N Shah, Neekhil A Patel, Samir A Matloob, Huan-Wee Chan, Edward W Dyson, Ahmed K Toma, Laurence Watkins  
National Hospital for Neurology and Neurosurgery, UK  
E-mail: jineks7@gmail.com

Fluids and Barriers of the CNS 2015, 12(Suppl 1):P12

**Introduction:** The landmark discovery that control of autonomic physiology could be 'learned' using biofeedback was first demonstrated with heart rate [1,2]. Biofeedback control has since been demonstrated with physiological variables such as regional cerebral blood flow, and end tidal carbon dioxide, with therapeutic application in conditions including migraine and epilepsy [3-6]. Here, we demonstrate for the first time, learned control of intracranial pressure (ICP), in a single patient using biofeedback of simultaneous ICP recordings via a Spiegelberg<sup>TM</sup> intracranial pressure monitor.

**Hypothesis:** Mindfulness of breathing, guided by analogue ICP biofeedback can be used to reduce ICP in patients with known idiopathic intracranial hypertension.

**Method:** A single patient, with a known history of idiopathic intracranial hypertension was trained to direct attention to their breathing, while simultaneously observing their ICP, as displayed on a analogue readout. The display was connected to a right frontal Spiegelberg intracranial pressure monitor. In addition to an explicit instruction to direct their attention to the passage of breath through their nostrils, and maintaining regular breathing, the patient was asked to reduce their ICP value as much as possible, including negative values. This was repeated over two days. Specifically they performed 3 sessions on the 1st day, and 2 sessions on the 2nd day – each session consisted of 5 blocks of 90s each of attempted ICP reduction using 'biofeedback-guided mindfulness', followed by 60s of rest.

**Results:** During 'biofeedback-guided mindfulness', the patient reduced their median ICP on both days i.e. session averages: Day 1 Median ICP 1.9, Day 2 Median ICP -2.63. Control values were obtained from the hour before and after the biofeedback sessions i.e. average: Day 1 Pre-biofeedback Median ICP 6.5, Post-biofeedback Median ICP 3.5, Day 2 Pre-biofeedback Median ICP 5.0 Post-biofeedback Median ICP 4.1 (Overall day averages, Day 1 Median ICP 5.9, Day 2 Median ICP 6.0).

**Conclusion:** Using mindfulness of breathing and biofeedback of simultaneous ICP recordings, we were able to train a patient to control their own ICP. Although this will require validation with more patients, it provides for the possibility of training volitional control and reduction of symptomatic increases in ICP.

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## P13

### Circadian rhythm in idiopathic normal pressure hydrocephalus

Andreas Eleftheriou<sup>1,3\*</sup>, Martin Ulander<sup>2,3</sup>, Fredrik Lundin<sup>1,3</sup>  
<sup>1</sup>Department of Neurology, University Hospital, Linköping, Sweden;  
<sup>2</sup>Department of Clinical Neurophysiology, University Hospital, Linköping, Linköping, Sweden; <sup>3</sup>Department of Clinical and Experimental Medicine (IKE), Linköping University, Sweden  
E-mail: andelef2002@yahoo.gr

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**Introduction:** The pathogenesis of idiopathic normal pressure hydrocephalus (iNPH) may take place in structures close to the cerebral ventricular system. Suprachiasmatic nucleus (SCN), situated close to the third ventricle, is involved in circadian rhythm and is therefore of interest to study. One of the main symptoms of iNPH is cognitive impairment. Diurnal disturbances are a well-known phenomenon of patients with dementia. Diurnal rhythm has never been studied in iNPH. The aim was to study any changes of the diurnal rhythm and diurnal activity amplitude, before and after shunt operation in iNPH-patients.

**Methods:** Twenty consecutive iNPH patients fulfilling the criteria of American iNPH guidelines from 2005, 9 males and 11 females, mean age 73 (49-81) years were included. The patients underwent a pre-operative clinical work-up including 10 meters walk time (w10mt) steps (w10ms), TUG-time (TUGt) and steps (TUGs) and for cognitive function an MMSE score was measured. In order to receive circadian rhythm data actigraphic recordings were performed using the SenseWear 2 (BodyMedia Inc Pittsburgh, PA, USA) actigraph. Cosinor analyses of accelerometry data were performed in "R" using non-linear regression with Levenburg-Marquardt estimation. Pre- and post-operative data regarding mesor, amplitude and circadian period were compared using Wilcoxon-Mann-Whitney test for paired data.

**Results:** Twenty patients were evaluated before and three month post-operatively. Motor function (w10mt, w10ms, TUGt, TUGs) was significantly improved while MMSE was not significantly changed (pre: 26/30; post: 27/30). Actigraphic measurements (mesor, amplitude and circadian period) showed no significant changes after the shunt operation.

**Conclusion:** This is the first systematic study of circadian rhythm in iNPH-patients. There were no significant changes in circadian rhythm after shunt surgery. This is in line with the results from our previous actigraphic study showing that the patients did not improve their ambulatory activity in spite of improved motor function. Cognition measured with MMSE remained unchanged. These findings underscore the need of more active post-operative rehabilitation.

#### P14

##### Biomechanical model of cerebral vascular dynamics and their effect on CSF dynamics

Christine Goffin\*, Lukas Theisgen, Klaus Radermacher  
RWTH Aachen University, Germany  
E-mail: goffin@hia.rwth-aachen.de  
*Fluids and Barriers of the CNS 2015, 12(Suppl 1):P14*

With advancing age venous wall thickness increases going along with a loss of elastic properties, the arterioles curl and capillary density decreases leading to a reduction of cross sectional area [1]. Even in healthy individuals these changes influence vascular and CSF dynamics, as a reduction of total cerebral blood flow, aqueduct and cervical stroke volume are reported [2]. In NPH these dynamics seem to be altered in a different way, as aqueduct stroke volume [2] and ICP amplitude are increased and arteriovenous delay is drastically reduced compared to normal aging [3]. However it is not clear in what way the described vascular alterations influence the pressure propagation inside the vessels and impact CSF dynamics.

So far no biomechanical model exists that investigates the influence of macroscopic and microscopic changes of cerebral blood vessels. That is why we put a model up for discussion that simulates vascular pressure propagation and enables the investigation of altered vascular properties in the context of NPH.

A Matlab Simulink model was developed reproducing each vessel section by a distensible compartment. Therefore the cerebral vascular tree was divided into 13 sections from carotid artery to venous sinuses and the pulsatile carotid artery and sinus pressure were inputted as Fourier series. The cross sectional area was varied according to literature data and flow resistance was implemented taking into account the rheological characteristics of blood. The Windkessel function and relaxation properties of vascular walls were integrated by a Voigt model, enabling the variation of wall properties for each section individually. Due to the distensible vessel walls each section interacts with the CSF compartment and autoregulation was implemented by a simple proportional controller. After parameterisation mean pressure and pressure amplitude in the vessel sections showed good accordance with literature values [4].

We have proposed a model of vascular dynamics that is able to identify the impact of altered vascular wall properties and structural changes.

Furthermore the effect of different arterial and venous input pressure profiles can be analysed. These parameter analyses are part of our ongoing research.

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#### P15

##### Differentiation of cerebrospinal fluid inflammatory biomarkers between neonatal post-hemorrhagic and congenital hydrocephalus

Gakwaya Habiyaremye<sup>1</sup>, Diego M Morales<sup>1</sup>, Clint D Morgan<sup>2</sup>, James P McAllister<sup>1</sup>, David D Limbrick<sup>1</sup>

<sup>1</sup>Department of Neurological Surgery, Division of Pediatric Neurosurgery, Washington University, St. Louis, MO, USA; <sup>2</sup>Vanderbilt University School of Medicine, Nashville, TN, USA

E-mail: habiyaremyeg@wudosis.wustl.edu

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**Introduction:** Neonatal Post-hemorrhagic hydrocephalus (PHH) develops partly due to an inflammatory process occurring after intraventricular hemorrhage whereas the majority of congenital hydrocephalus (CH) results from primary and secondary CNS malformations. We hypothesize that cerebrospinal fluid (CSF) content of inflammatory biomarkers is higher in neonatal PHH relative to CH. To test this hypothesis, we measured CSF concentrations of CCL-3, CXCL-12, CX3CL-1, IL-10 and P-selectin in both conditions.

**Methods:** ELISA was used to measure CSF inflammatory biomarker concentrations in 10-15 patients per study group. Study groups included PHH-LP (lumbar puncture), congenital hydrocephalus (CH), and pre-term controls (PT). PHH-LP and PT samples were collected perinatally during spinal tap; CH samples were collected ventricularly at time of reservoir implantation.

**Results:** CCL-3 was significantly increased in PHH relative to both CH and PT (PHH-LP>CH with p= 0.0002; PHH-LP>PT, p=0.0001). P-selectin was significantly elevated in PHH compared to CH and PT (PHH-LP>CH, p=0.0002; PHH-LP>PT, p=0.0009). IL-10 was significantly elevated in PHH-LP relative to PT (PHH-LP>PT, p=0.0001). No significant differences were

found in CXCL-12 and CX3CL-1. Study group comparison did not show any difference between CH and PT.

**Conclusions:** Our findings suggest that PHH may be distinguished from CH based on its higher levels of CCL-3 and P-selectin. However, CX3CL-1, CXCL-12 and IL-10 may not be useful in distinguishing both conditions. Interestingly, it appears that CH may not be distinguished from PT controls based on levels of inflammatory biomarkers. These findings confirm our hypothesis that inflammatory biomarkers are higher in neonatal PHH and indicate that the use of inflammatory modulators could be more beneficial to PHH versus CH.

#### P16

##### A proposal to explain "covert" increases in intracranial pressure

Doug Hamilton, Mark Hamilton\*, Alim Mitha, John Tyberg  
University of Calgary, Calgary, Canada  
E-mail: mghamilton.random@gmail.com  
*Fluids and Barriers of the CNS* 2015, **12(Suppl 1):P16**

**Introduction:** Some substantial number of unfortunate patients suffer from the symptoms and signs of elevated cerebrospinal fluid (CSF) pressure, even though pressure measured in the cerebral venous system is normal. We hypothesize that, with elevated CSF pressure, cerebral microvascular congestion may occur, even though (subdural) large-vein pressure has been shown to be normal.

**Background:** Even with elevated CSF pressure, large-vein pressure could be normal because the large veins are "tenting" open by their structural relation to the dura. However, the smaller, penetrating veins are not protected by the dura in this way so they could collapse. By this "Starling-resistor" action, venular and microvascular pressure would have to increase if flow were to continue. This increased microvascular pressure might be measured by an adaptation of cardiologists' wedge-pressure logic. (When an artery is obstructed by a catheter or by the inflation of a balloon, the pressure measured in the stationary column of blood beyond the obstruction is equal to the downstream pressure.)

**Hypothesis:** These concepts are illustrated in the figure. Solid lines indicate the relationships of intravascular pressure when CSF pressure is normal (~10 mmHg). Dashed lines indicate the relationships when CSF pressure is elevated (~35 mmHg). If flow is to continue, the pressure in the capillaries and in the small penetrating veins must exceed CSF pressure. However, pressure in the large "dura-strutted" veins will continue to be normal and to be governed only by right atrial pressure.

**Conclusion:** Experimental verification of this hypothesized mechanism has been impeded by the presence of an arterial rete in many species other than in dogs or in human subjects and dogs have been unavailable to us. Even in the absence of experimental verification, we suggest that these concepts have important therapeutic implications: normal dural vein pressure should NOT rule out elevated CSF pressure and alternative measures of CSF pressure should be employed.

**Consent to publish:** Written informed consent for publication of their clinical details was obtained from the patient.

#### P17

##### eGFR in CSF-flow disorders - a representation of comorbid state or an element of the underlying pathophysiology?

Patricia Haylock-Vize\*, Claudia Craven, Edward Dyson, Chari Aswin, Samir A Matloob, Andrew Stevens, Simon D Thompson, Syed N Shah, Tarek Moustafa, Neehil A Patel, Huan Wee Chan, Jinendra Ekanayake, Ahmed K Toma, Laurence D Watkins  
The National Hospital for Neurology and Neurosurgery, UK  
E-mail: patriciahaylockvize@gmail.com  
*Fluids and Barriers of the CNS* 2015, **12(Suppl 1):P17**

**Introduction:** All cause mortality increases with lower levels of estimated glomerular filtration rates. As part of a comorbidity focus, we assessed the eGFR in CSF-flow disorder patients guided by NICE recommendations, current literature recognising a relative hazard ratio per 15mls/min decrease in eGFR of 1.04[1] and consideration of the 2010 Chronic Kidney Disease Epidemiology Collaboration eGFR categories.

**Methods:** 182 CSF-flow disorder patients who had eGFR measurement were grouped into the respective subtypes; IIH (n=41), NPH (n=72), CSF

hypovolaemia (n=7) and other causes (n=45). Others included those investigated for NPH but found not to be suitable for shunt.

Estimated GFR was categorised as per NICE guidelines; (ml/min/1.73m) in line with current clinical laboratory facilities;

>90 normal high, .

60-89 mild reduction related to normal range for a young adult, .

45-59 mild-moderate reduction, .

30-44 moderate-severe reduction, .

15-29 severe-reduction, .

<15 kidney failure.

The eGFR's were recorded and the mean calculated for each subgroup.

**Results:** IIH cohort; mean eGFR 77.73;

26 patients >90 normal high, 14 patients in 60-80 mild reduction, and 1 patient 45-59 mild-moderate category.

Primary NPH; mean eGFR 73.32mls/min; 18 patients >90 normal high, 35 patients 60-89 mild reduction, 17 patients 45-59 mild-moderate and 2 patients 30-44 moderate-severe category.

Secondary NPH; mean eGFR 81.94mls/min; 16 patients 60-89 mild reduction range and 1 patient 45-59 mild-moderate category.

Orthostatic HA; mean eGFR 87.25mls/min; 5 patients >90 normal high and 2 patients 60-89 mild reduction.

Other cohort; mean eGFR 76.96mls/min; 22 patients >90, 21 patients 60-89 mild reduction and 2 patients 45-59 in the moderate-severe reduction.

Of the 182 patients, 71 patients had high normal eGFRs >90mls/min representing 39% of patients. 48% fell into the 60-89 mild reduction range, 11.5% into the 45-59 mild-moderate reduction range and 1% into the moderate-severe reduction range.

**Conclusions:** A reduced estimated GFR is commonly seen in the CSF-flow disorders patient cohorts. Given the emphasis towards comorbidity factors influencing surgical outcomes, this acts as a marker of comorbidity and physiological reserve for surgical tolerance and post-operative performance and should therefore be taken into consideration.

The altered eGFR could represent the comorbid state of the patient or it could form an element of the underlying pathophysiology of CSF-flow disorders or indeed both. Larger studies are required with more translational medical research models.

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#### P18

##### Comorbidities in NPH - local introspective - 'Shunt them all!'

Patricia Anne Haylock-Vize\*, Eleanor Carter, Syed Shah, Claudia Craven, Aswin Chari, Simon Thompson, Edward W Dyson, Samir Matloob, Andrew Stevens, Huan Wee Chan, Jinendra Ekanayake, Ahmed Toma, Michelle Leemans, Laurence D Watkins  
The National Hospital for Neurology and Neurosurgery, UK  
E-mail: patriciahaylockvize@gmail.com

*Fluids and Barriers of the CNS* 2015, **12(Suppl 1):P18**

**Introduction:** In response to the 2013 ISH-CSF task force review on comorbidities in NPH we assessed 73 patients who were diagnosed with NPH and underwent shunt surgery at our tertiary neurosurgical unit between August 2008 and August 2012.

**Method:** Data was collected as a retrospective case analysis and converted to the ICD-10 Charlson Comorbidity Index (CCI) which predicts the ten-year mortality for a patient with a range of comorbid conditions and the American Society of Anaesthesiologists (ASA) grade.

Factors assessed past medical history, polypharmacy, pre-operative haemoglobin, duration and NPH symptoms, exercise tolerance, functional ability, complications, care level of admission, length of stay, destination on discharge and allied health professional input.

**Results:** CCI average was 5.5 with a range of 3 - 10 (Mild CCI 1-2, moderate CCI 3-4, Severe CCI >5).

ASA average was 2.66 ranging from 2-4.

Over a 4 year period, this patient group amassed 573 hospital days with an average of 8.18 days each patient ranging from a minimum of 3 days to a maximum of 26 days.

Discharge destination; 61 (83.56%) patients went straight home from point of discharge, 6 (8%) patients were admitted to rehabilitation unit, 3 (4%) patients returned to their referring hospital, 1 patient returned to a nursing home and 1 patient returned to sheltered accommodation.

11 (15%) patients were dependent for all ADLs, 43 (59%) patients required help with ADLs and 20 (27%) patients were fully independent.

Only 2 patients did not require any allied health care professional input during their stay indicating 97% of these patient do require AHP in put. 43% have had their presenting symptoms for less than 12 months at the time of treatment. 68% had symptoms for 24 months at time of treatment.

**Conclusion:** Our NPH patient cohort present with a severe CCI score necessitating adequate neuroanaesthetic pre-operative review and work up. Most neurosurgical units exclude patients for shunt based on comorbidity, yet our data indicates our group of patients to be a complex group who we do not exclude based on comorbidity where they have demonstrated a good response to simulated shunt through extended lumbar drainage protocol.

This patient group rely heavily on Allied Healthcare Professionals in correlation with their in-patient episode.

Most patients (68%) received treatment within 2 years of symptom onset demonstrating capacity to target patents in the less than 1 year symptom onset time period.

By understanding the needs of our NPH patient population it puts us in a better position to design our service to support our patient needs and facilitate an optimal hospital episode.

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#### P19

##### Endoscopic resection of colloid cyst: long-term followup with 63 patients

Albert Isaacs\*, Walter Hader, Mark Hamilton

University of Calgary, Canada

E-mail: akm.isaacs@gmail.com

Fluids and Barriers of the CNS 2015, 12(Suppl 1):P19

**Introduction:** Colloid cysts of the third ventricle are rare, histologically benign lesions that can be associated with obstructive hydrocephalus. Endoscopic removal developed as an alternative to microsurgical craniotomy as a less invasive surgical treatment. This review examines the endoscopic surgical experience for a consecutive series of patients with colloid cyst of the third ventricle.

**Methods:** Patients with a diagnosis of "colloid cyst of the third ventricle" who were treated in Calgary between January 1994 and July 2014 were reviewed using a clinic database and registry.

**Results:** 93 patients were identified. 30 patients without hydrocephalus underwent serial MRI and clinical observation with one patient developing hydrocephalus leading to surgical treatment. 63 patients underwent endoscopic treatment of their colloid cyst (male=34; female=29). The mean age at diagnosis was 46.3 years. 2 patients had been previously treated with other surgical approaches. All surgically treated patients had hydrocephalus and hydrocephalus resolved in all 63 patients. 1 patient sustained an injury to the internal capsule with transient hemiparesis. Mean followup was 8.8 years (range 0.1-20.2 years). 2 patients experienced colloid cyst recurrence treated with a second endoscopic removal.

**Conclusion:** Endoscopic treatment of third ventricle colloid cysts can be performed with low risk as an alternative to microsurgical resection.

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#### P20

##### Change of Virchow-Robin spaces in idiopathic normal pressure hydrocephalus and its pathogenetic significance

Masatsune Ishikawa\*, Shigeki Yamada, Kazuo Yamamoto

Rakuwakai Otowa Hospital, Japan

E-mail: rakuwadr1001@rakuwadr.com

Fluids and Barriers of the CNS 2015, 12(Suppl 1):P20

**Introduction:** Idiopathic normal pressure hydrocephalus (iNPH) is a disorder of aged adults, but its pathogenesis is still unknown. Recently, Virchow-Robin Spaces (VRS) are interested in anatomical structure for interaction between interstitial fluid (ISF) and cerebrospinal fluid (CSF). VRS are known to observe mainly in the basal ganglia and the subcortical white matter and they increase in number with aging. In the present study, we investigated morphological features of VRS in the brain in the aged healthy adults and patients with probable iNPH.

**Methods:** Using 3-T MRI and constructive interference in steady state (CISS), 10 healthy aged adults and 30 patients with probable iNPH were examined on morphological features of VRS in the basal ganglia and subcortical white matter.

**Results:** VRS in the basal ganglia were curved, irregularly sized and shaped, and communicated with the cerebrospinal fluid in the subarachnoid space; they contained perforating arteries. VRS in the white matter were straight, smooth, homogeneously sized and shaped, and did not penetrate the cortex. Arteries were not seen in VRS of the white matter. White matter VRS were sparse in patients with iNPH. Postoperatively after shunt surgery, VRS in the white matter were mildly decreased in diameter, but not in number. No significant changes were noted in basal ganglia VRS.

**Conclusions:** Morphological features of VRS in the basal ganglia and white matter were different. VRS in the basal ganglia were seen as genuine perivascular spaces; while neither communication with subarachnoid spaces nor arteries were seen in white matter VRS, even by 3D-CISS sequences and high-resolution magnetic resonance angiography on 3T-MRI. White matter VRS were sparse in patients with iNPH and they were mildly decreased in diameter, but did not change in number after surgery. They may be due to dilated ISF spaces or secondary changes of amyloid deposition in the leptomeningeal arteries, or both. Further studies are necessary to elucidate the functional role of VRS in normal subjects and patients with iNPH.

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#### P21

##### Surgical treatment results and pathological features in pediatric occult tight filum syndrome

Jeff Julian<sup>1</sup>, Michael Punsoni<sup>2</sup>, John Donahue<sup>3</sup>, Ed Stopa<sup>4</sup>, Petra M Klinge<sup>5\*</sup>

<sup>1</sup>Neurosurgical Department, Rhode Island Hospital, USA; <sup>2</sup>Neuropathology, Rhode Island Hospital, USA; <sup>3</sup>Neuropathology, Rhode Island Hospital, USA;

<sup>4</sup>Neuropathology, Rhode Island Hospital, USA; <sup>5</sup>Neurosurgical Department, Rhode Island Hospital, USA

E-mail: pklinge@lifespans.org

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**Introduction:** Occult tight filum terminale syndrome (OTCS) is defined as a clinical syndrome of tethered cord and without "classic" radiographic evidence of low lying conus and/or fatty filum.

**Methods:** A consecutive series of 11 children (2-17 years) diagnosed with tethered cord syndrome (Triad of neurological, urological and orthopedic findings) since 2010, a non-diagnostic MRI, underwent microsurgical



resection of the filum. Presenting symptoms and symptoms most responsive to surgery, imaging and pathology of the filum were analyzed. **Results:** OTSC show the overall improvement in all dimensions of the clinical syndrome, e.g. scoliosis, walking and falling spells, incontinence and overall activity level due to improved pain. Increased tone in the lower extremities and foot deformities appeared as a negative predictor of improvement. Associated syringohydromyelia did not show any change in the 1 year follow-up MRI despite marked clinical improvement. Pathology shows a variety of features including "nerve twigs".

**Conclusions:** The accuracy of the clinical TRIAD consisting of symptoms in the dimensions of bowel and bladder dysfunction, orthopedic and neurological signs to define "occult filum terminale or occult tight filum syndrome" and the accuracy of the clinical TRIAD to predict surgical success of detethering has to be explored and proven in a prospective fashion.

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#### P22

##### An effective technique for preventing the subcutaneous migration of the abdominal lumboperitoneal shunts catheters

Takashi Kawahara<sup>1\*</sup>, Masamichi Atsuchi<sup>2</sup>, Hiroshi Tokimura<sup>3</sup>, Tetsuzo Tomosugi<sup>1</sup>, Kazuho Hirahara<sup>1</sup>, Kazunori Arita<sup>3</sup>

<sup>1</sup>Department of Neurosurgery, Kagoshima City Hospital, Kagoshima, Japan;

<sup>2</sup>Division of Neurosurgery, Atsuchi Neurosurgical Hospital, Kagoshima, Japan;

<sup>3</sup>Department of Neurosurgery, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan

E-mail: t.kappara@gmail.com

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**Introduction:** Migration of the lumboperitoneal shunt catheter into the abdominal subcutaneous space is not uncommon. We devised a new simple method (Transrectal Gap method we call) for installment of peritoneal tube aiming to prevent the migration.

**Methods:** After catheter insertion into the lumbar spinal subarachnoid space peritoneal side tube was drawn into areola vertical space between abdominal fat and superficial fascia of rectus muscle. After a 4 cm incision on the superficial rectal fascia and split the rectus muscles, the tip of catheter was obliquely passed through abdominal rectus muscle using mosquito clamp. The tube was then inserted into abdominal cavity through a small hole on the deep fascia and peritoneal membrane which was 3 cm down to the hole on anterior rectal sheath.

**Results:** Thus, the peritoneal side catheter ran obliquely, upper lateral to lower medial, through anterior sheath, abdominal rectus muscle, and inserted to the peritoneum. We have so far operated 120 patients with this method without major complication or migration of the catheter.

**Conclusion:** This technique installs the abdominal catheter run parallel to the abdominal wall. As the result, the influence of the abdominal pressure to the abdominal catheter seems reduced. And the catheter does not pass the dead space made by operation, it is another reason preventing the subcutaneous migration.

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#### P23

##### Normal pressure hydrocephalus – why treatment is often delayed or not even initiated

Uwe Kehler

Asklepios Hospital Hamburg Altona, Germany

E-mail: u.kehler@asklepios.com

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Normal pressure hydrocephalus is a common disease in elderly people and treatment is beneficent. It is also well known, that delayed treatment of NPH shows worth results than early treatment. However, many patients are sent with enormous delay and or not even sent to hydrocephalus specialists. The aim of this work is to search for the reasons and discuss improvements.

**Methods:** The reasons for delayed treatment of NPH in patients who were treated finally in our department are summarized. Only reasons which occurred twice are mentioned not to overestimate too exceptional cases. Only cases were included who improved after shunt surgery.

**Results:** The reasons for delayed NPH treatment could be identified: 1: Spinal tap testing did not show clear improvement, although patient felt substantial improvement. 2: Examination of spinal tap test was done at wrong time, patient improved substantially after demission of the hospital. 3: Radiologist misdiagnosed hydrocephalus (typical wrong diagnosis: brain atrophy and/or cerebral micro-angiopathy), 4: Patient was considered to be too old for shunt surgery. 5: General physician and/or neurologist considered surgery too risky (without explaining the patient the progressive natural history of the disease). 6. NPH was not suspected by the general physician and/or neurologist or NPH was misdiagnosed as Alzheimer's disease and Parkinson's disease.

**Discussion:** Unawareness of NPH, general physician's and neurologist's fear of shunt complications, thoughtless radiological diagnosis of brain atrophy with excluding hydrocephalus are some reasons why patients are sent delayed to hydrocephalus specialists. Medical education and information has to be improved that NPH patients can get the benefit of treatment as early as possible.

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## P24

### Cerebrospinal fluid dynamics at the lumbosacral level in patients with spinal stenosis

Keewon Kim<sup>1\*</sup>, Dong-Joo Kim<sup>2</sup>, Kwang Dong Kim<sup>1</sup>, Hack-Jin Lee<sup>2</sup>,  
Chul-Ho Sohn<sup>1</sup>, Sun-Gun Chung<sup>1</sup>, Se-Woong Chun<sup>1</sup>, Ho NamKoong<sup>1</sup>

<sup>1</sup>Seoul National University Hospital, Korea, Republic of (South Korea);

<sup>2</sup>Department of Brain and Cognitive Engineering, Korea University, Korea, Republic of (South Korea)

E-mail: keewonkimm.d@gmail.com

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**Introduction:** The hydrodynamics of the cerebrospinal fluid (CSF) is well-known to contribute to neurological disorders of the brain. However, little attention has been paid to the CSF dynamics in the lumbosacral spine. Meanwhile, the pathomechanism of neurogenic claudication, a characteristic symptom of spinal stenosis, has not been clearly elucidated. In this study, we suspected that spinal stenosis may be associated with altered CSF dynamics and compared CSF flow velocities at the lumbosacral spinal level between patients with spinal stenosis and healthy controls, at rest and at claudication.

**Methods:** Twelve subjects (4 patients with spinal stenosis and 8 healthy controls; 25-77 years old; 7 males) underwent phase-contrast magnetic resonance imaging (PC-MRI) to quantify CSF dynamics at the lumbosacral spinal level. Using PC-MRI, the CSF flow velocities were measured at the L2 and S1 levels. All of the subjects underwent PC-MRI at rest and after walking (to provoke neurogenic claudication in the patients).

**Results:** The flow rate in the sacral spine (caudal peak flow:  $-0.25 \pm 0.28$  cm/s) was greatly attenuated compared to the flow in the lumbar spine (caudal peak flow:  $-0.93 \pm 0.46$  cm/s) in both patients and controls. The caudal peak flow was slower in patients ( $-0.65 \pm 0.22$  cm/s) than controls ( $-1.07 \pm 0.49$  cm/s). The difference between the L2 caudal peak flow became more pronounced after walking ( $-0.66 \pm 0.37$  cm/s in patients,  $-1.35 \pm 0.52$  cm/s in controls;  $p = 0.028$ ). The sacral CSF flow after walking was barely detectable in patients (caudal peak flow:  $-0.09 \pm 0.03$  cm/s) compared with controls (caudal peak flow:  $-0.32 \pm 0.26$  cm/s). The severity of structural stenosis (area or AP diameter of the spinal canal) did not correlate with the flow velocities within the participants.

**Conclusions:** CSF dynamics in the lumbosacral spine were more attenuated in patients with spinal stenosis than healthy controls in a manner that was not proportionate to the structural stenoses. After walking, the CSF flow rate did not exhibit an appropriate increase in patients experiencing claudication, whereas the flow rate did increase appropriately in controls. Altered CSF dynamics may partially explain the pathophysiology of spinal stenosis.

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## P25

### Surgical indication of iNPH (idiopathic normal pressure hydrocephalus)

Teruo Kimura<sup>1</sup>, Toshihide Sugimura, Shin Fukuda, Makoto Miyano, Masaaki Hashimoto

Dohtoh Neurosurgical Hospital, Okhotsk Cerebrovascular Center, Japan

E-mail: tekimura-nsu@umin.ac.jp

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**Introduction:** Some patients with iNPH often can recover independent ADL and can be easily rehabilitated after shunt surgery. However, other patients sometimes cannot recover independent ADL even if improvement is obtained after treatment, because of some factors. The purpose of this study is to examine the influence of the factor determining the benefit from shunt surgery.

**Methods:** All patients underwent a tap test during 9 years from 2002 to 2010, and 154 probable iNPH patients who showed a clinical improvement of at least 10% underwent shunt placement (V-P shunt, 12 patients; L-P shunt, 142 patients). One hundred and thirty-three patients who could be followed up for one year were investigated for age, the interval from onset to surgery, severity, degree of improvement by tap test, MRI findings (DESH or non-DESH).

**Results:** According to older patients, the postoperative recovery of mRS, gait disturbance (GD), dysuria, and cognitive impairment (CI) was poor. According to long interval from onset to surgery (group 1 < 2 < 3 < 4 < 5), the score (mRS, iNPHGS) of them showed higher points mean more severity. There were correlations between the length of the interval from onset to surgery and severity ( $P < 0.01$ ), between the length of the interval from onset to surgery and the degree of improvement after surgery ( $P < 0.01$ ), and between severity and the degree of improvement after shunt ( $P < 0.01$ ). There were correlations between severity of GD ( $P < 0.01$ ) and the degree of improvement after surgery. In tap test, the patient (group A) of remarkable recovery of postoperative score, the symptom was improved, especially, mRS, GD significantly ( $P < 0.01$ ), keeping good ADL after one year ( $p < 0.01$ ). The patient with DESH in preoperative MRI findings (coronal view) was more improvement than patients with non-DESH in mRS, GD, dysuria and CI, significantly ( $p < 0.01$ ), keeping good independent ADL after one year postoperatively.

**Conclusions:** Surgical indication is decided with careful consideration of social indication including the comorbidity, fully informed consent should be made.

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## P26

### Controversies in the management of craniosynostosis at an advanced age

Petra M Klinge<sup>1\*</sup>, Rajiv Iyengar<sup>2</sup>, Stephen Sullivan<sup>3</sup>, Wendy Chen<sup>4</sup>, Jerrold Boxerman<sup>5</sup>, Helena Taylor<sup>6</sup>

<sup>1</sup>Department of Neurosurgery, Rhode Island Hospital, USA; <sup>2</sup>Department of Plastic Surgery, Rhode Island Hospital, USA; <sup>3</sup>Department of Plastic Surgery,

Rhode Island Hospital, USA; <sup>4</sup>Department of Pediatric Ophthalmology, Rhode Island Hospital, USA; <sup>5</sup>Department of Neuroradiology, Rhode Island Hospital, USA; <sup>6</sup>Department of Plastic Surgery, Rhode Island Hospital, USA  
E-mail: pklinge@lifespan.org  
*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:P26

**Introduction:** In this study, we describe a cohort of patients with a delayed presentation of non-syndromic craniosynostosis.

**Methods and patients:** 10 consecutive patients with delayed diagnosis and treatment of craniosynostosis between January 2008 and February 2015 were included. Inclusion criteria were age greater than two years at time of initial evaluation, fusion of at least one suture, and adequate imaging studies including CT or MRI or both. All children were evaluated by a multidisciplinary team including a craniofacial plastic surgeon, neurosurgeon, ophthalmologist, neuroradiologist, developmental specialist and medical geneticist. Either intraparenchymal ICP monitoring was performed for 24-48 hours or intraoperative epidural ICP monitoring at the time of surgery.

**Results:** Headaches were improved in all patients and the most reliable symptom. The comparative perioperative data (median estimated blood loss, operative time and hospital stay) between reconstructions on infants versus older children Delayed surgery required greater median operative time, but median blood loss and duration of hospital stay were comparable. There were no complications (e.g. return to OR, prolonged intubation) in either this cohort or the infant controls.

**Conclusion:** While the debate rages over the functional utility of cranial vault remodeling for non-syndromic craniosynostosis, this series suggests a high rate of morbidity in neglected cases. Seven out of ten children had documented developmental delay, five out of ten had Chiari malformations, and five out of ten had debilitating headaches. Three presented with documented ICP elevation. This series suggests that delaying cranial vault reconstruction for craniosynostosis is associated with a high incidence of developmental delay, headaches and coincident Chiari malformations. Delayed reconstruction and cranial vault expansion can be performed for these older patients with low morbidity but added operative time.

## P27

### The NPH radscale; a new radiological scale for evaluation of suspected normal pressure hydrocephalus

Karin Kockum<sup>1\*</sup>, Elna-Marie Larsson<sup>2</sup>, Otto Lilja-Lund<sup>1</sup>, Michelle Rosell<sup>1</sup>, Lars Söderström<sup>3</sup>, Johan Virhammar<sup>4</sup>, Katarina Laurell<sup>1</sup>

<sup>1</sup>Department of Pharmacology and Clinical Neuroscience, Unit of Research, Education and Development, Östersund, Umeå University, Sweden;

<sup>2</sup>Department of Surgical Sciences, Radiology, Uppsala University, Sweden;

<sup>3</sup>Unit of Research, Education and Development, Östersund Hospital, Region Jämtland Härjedalen, Sweden; <sup>4</sup>Dept of Neuroscience, Neurology, Uppsala University Hospital, Sweden

E-mail: kockum.karin@gmail.com

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**Introduction:** Imaging of the brain with computerized tomography (CT) or magnetic resonance imaging (MRI) is crucial to support the diagnosis of normal pressure hydrocephalus (NPH). The aim of this study was to construct a radiological scale, composed of morphological signs of NPH, and compare with an existing scale for clinical NPH symptoms developed by Hellström et al[1].

**Methods:** In a prospective population-based study of the prevalence of NPH, 91 individuals (43 males), mean age 74 years (range 66-92 years), underwent CT of the brain and neurological examination with assessment of clinical symptoms. A radiological scale consisting of eight radiological parameters was developed and correlated with the clinical NPH scale score to yield a reliable diagnostic tool. Two independent radiologists, blinded to clinical data, visually assessed and performed all measurements of the parameters Evans index >0.3, callosal angle <90°, narrow high convexity sulci, focally dilated sulci, dilated Sylvian fissures, focal bulging of ventricular roof, dilated temporal horns, and periventricular hyperintensities. After conversion into points, the parameters were summarized yielding a score ranging from 0 to 10 points where higher scores indicates more severe radiological changes.

**Results:** Mean clinical NPH score was 83 (min 30, max 100, SD=17). Mean NPH radscale was 2 (min 0, max 10, SD=2). There was a significant

correlation ( $rs=0.5$ ,  $p<0.0001$ ) between the new NPH radscale and clinical NPH symptoms as assessed by the NPH symptom scale.

**Conclusion:** The new NPH radscale seems to be a promising tool for diagnosing NPH.

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## P28

### Magnesium sulfate treatment for juvenile ferrets following induction of hydrocephalus with kaolin

Domenico Luciano Di Curzio<sup>1,2\*</sup>, Emily Turner-Brannen<sup>1,2</sup>, Xiaoyan Mao<sup>1,2</sup>, Marc Del Bigio<sup>1,2</sup>

<sup>1</sup>University of Manitoba, Canada; <sup>2</sup>Children's Hospital Research Institute of Manitoba, Canada

E-mail: umdicur@myumanitoba.ca

*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:P28

**Introduction:** Hydrocephalus is characterized by altered cerebrospinal fluid flow increasing brain ventricular cavities. Rodent studies showed that axonal pathology includes calcium-mediated proteolysis, which can be reduced by the calcium channel antagonist magnesium sulfate (MgSO<sub>4</sub>). Hydrocephalic ferrets show similar neurological changes as rodents and humans, and thus MgSO<sub>4</sub> treatment was tested in juvenile ferrets.

**Methods:** Fourteen-day old ferrets were given kaolin injections into the cisterna magna. Magnetic resonance imaging was performed two weeks later to assess ventricle size and stratify ferrets into treatment groups. Ferrets were treated for two weeks with MgSO<sub>4</sub> or saline, and then imaged before sacrifice. Behaviour was examined thrice weekly. Histological and biochemical assays were also performed.

**Results:** Compared to controls, hydrocephalic ferrets were not appreciably different in terms of weight and behaviour; however, those receiving MgSO<sub>4</sub> weighed less, were more lethargic, and displayed reduced activity than those receiving saline. Hydrocephalic ferrets developed ventriculomegaly, but there were no differences for either treatment group. They also exhibited cerebral thinning, decreased depth of cerebral sulci, and rarefaction and fragmentation of periventricular white matter. Though glial fibrillary acidic protein content was elevated in saline treated ferrets, indicative of reactive astroglial changes, there were no significant differences compared to MgSO<sub>4</sub> treated ferrets nor to controls. Myelin basic protein content and myelin enzyme activity also displayed no significance differences between treatment groups.

**Conclusions:** Hydrocephalus-induced disturbances are not ameliorated by MgSO<sub>4</sub> treatment. This suggests that unlike rodents, hydrocephalic ferrets do not experience behavioural improvements nor white matter protection from MgSO<sub>4</sub> therapy, which may be the case for humans with even more complex brains.

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## P29

### Clinically relevant skull models and optical measurement method to evaluate programmable hydrocephalus valve tool kit usability

MA Luedtke<sup>1\*</sup>, AJ Dextradeur<sup>1</sup>, TB Boden Jr<sup>1</sup>, J Mowry<sup>1</sup>, JV Pattisapu<sup>1</sup>, JT Megerian<sup>2</sup>

<sup>1</sup>Codman Neuro, Raynham, MA, USA; <sup>2</sup>Anavir Pharmaceuticals, Aliso Viejo, CA, USA

E-mail: mluedtk@its.jnj.com

*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:P29

**Introduction:** Five simulated skull models were created to simulate typical clinical conditions experienced while programming implanted adjustable ventriculoperitoneal hydrocephalus shunt valves. These models were created with physician feedback and evaluated by 13 health care professionals. Based on tactile evaluations and qualitative feedback, three models were selected as most clinically relevant. An optical measurement

and valve setting method were developed to characterize programming tool movements during valve programming procedure and usability testing that evaluated over 50 health care professionals that program hydrocephalus valves.

**Methods:** The skull models used a variety of synthetic tissues and thicknesses simulating a 3mm scalp thickness protruding valve model (such as younger or older patients with thin skin), a 7mm scalp thickness model (that characterizes 'average' patients) and a 10mm thick model (simulating post-surgical edema or tissue scarring over a valve implanted for years). Different colors of ultraviolet fluorescent invisible ink markers were used to draw dot pairs relative to the valve center. Precision drilled tool kits (precision machined pairs of holes) were developed to characterize angular offset in addition to actual offset from valve center. Models were covered in plastic wrap enabling the same models to be reused throughout usability studies minimizing error. Various cameras were used (video and still) with visible and ultraviolet light photography throughout usability testing.

**Results:** The printed grid overlays were on average 0.05mm +/- 0.35 mm offset compared to the drawing; The machined toolset hole centers were on average -0.03mm +/- 0.40 mm offset compared to the drawing; The markers dots were on average 0.15mm +/- 0.30 mm offset compared to the drawing; The valve center was on average 0.43mm +/- 0.22mm offset from the printed grid overlay and had a difference in angle of -0.26 +/- 1.37 degrees from the actual position of the valve. Real time valve setting was enabled with an endoscope placed underneath the programmable valve.

**Conclusions:** It is very important to accurately characterize human factors while developing medical devices. Clinically relevant models and these measurement methods enabled characterization of programmable hydrocephalus valve tool kit usability.

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#### P30

##### Infratentorial intracranial pressure monitoring: a hazardous option or an indispensable post-operative tool?

Romain Manet<sup>1\*</sup>, Laurent Gergele<sup>2</sup>, Benjamin Pommier<sup>1</sup>, Olivier Testa<sup>1</sup>, Christophe Nuti<sup>1</sup>, François Vassal<sup>1</sup>, Jérôme Morel<sup>2</sup>

<sup>1</sup>Department of Neurosurgery, University hospital of Saint-Etienne, France;

<sup>2</sup>Department of Anesthesiology and Intensive Care, University hospital of Saint-Etienne, France

E-mail: [romain.manet@neurochirurgie.fr](mailto:romain.manet@neurochirurgie.fr)

Fluids and Barriers of the CNS 2015, 12(Suppl 1):P30

**Introduction:** Due to its restricted size and the critical structures it contains, the posterior cranial fossa (PCF) is challenging for the neurosurgeon and each procedure exposes the patient to early and dramatic post-operative supratentorial (acute hydrocephalus) and/or infratentorial (brain swelling and/or hemorrhage) complications. Patient's monitoring after infratentorial surgery remains challenging. Indeed, supratentorial Intra Cerebral Pressure (ICPs) monitoring may not reflect infratentorial ICP (ICPi). Moreover, early post-operative CT scan is often difficult to interpret and occurrence of complications is lately suspected in the presence of clinical signs of brainstem impairment (bradycardia, pupillary dilation).

**Material and methods:** Case report. Literature review.

**Results:** We report the illustrative case of a 64 years old woman presenting severe bradycardia and bilateral mydriasis a few hours after a schedule infratentorial procedure. The CTscans reported cerebellar swelling and acute hydrocephalus. A second look surgery was performed for external ventricular drainage (EVD) and PCF decompression. ICP measured through EVD (ICPs) was low (5mmHg). Tactile estimation of intradural pressure was uncertain. Then a transdural intraparenchymal ICP transducer (ICPi) was inserted within the operated cerebellar hemisphere. During the initial post-operative course, monitoring showed significant difference between ICPi and ICPs during the first 24 hours (mean ICPi 17.2 mmHg +/- 2 vs mean ICPs 9.3 mmHg +/- 4.5) and during the 4 days after (mean ICPi 14.6 mmHg +/- 2.9 vs mean ICPs 7.8 mmHg +/- 3.1). The patient presented two episodes of severe bradycardia, with concomitant raise of ICPi above 20 mmHg (without significant change of ICPs and no over-drainage through EVD), treated successfully with osmotherapy. By means of optimisation of cerebral perfusion pressure (CPP) according to ICPi, patient was discharged of the Intensive Care Unit after 10days with moderate disability (GCS15, mRS4), and no complication of ICPi monitoring (no CSF leak).

**Conclusion:** Due to "ancestral" fear of neurosurgeons to perform PCF drainage or ICP monitoring, in relations with former descriptions of major complications, ICPi monitoring remains a controversial and confidential practice. However, supratentorial ICP monitoring and hydrocephalus management can fail to prevent life threatening complications after infratentorial surgery or others PCF insults and ICPi monitoring should be evaluated to optimize post-operative management.

#### P31

##### External hydrocephalus in adults: an insidious cause of delayed intracranial hypertension. Report of 33 relevant cases treated with success by CSF lumbar drainage

Romain Manet<sup>1\*</sup>, Romain Guerin<sup>2</sup>, Orianne Martinez<sup>3</sup>, Gilles Francony<sup>2</sup>, Jean-Paul Roustan<sup>3</sup>, Jean-François Payen<sup>2</sup>, Serge Molliex<sup>4</sup>, Jérôme Morel<sup>4</sup>, Laurent Gergele<sup>4</sup>

<sup>1</sup>Department of Neurosurgery, University hospital of Saint-Etienne, France;

<sup>2</sup>Department of Intensive Care, University hospital of Grenoble, France;

<sup>3</sup>Department of Intensive Care, University hospital of Montpellier, France;

<sup>4</sup>Department of Intensive Care, University hospital of Saint-Etienne, France

E-mail: [romain.manet@neurochirurgie.fr](mailto:romain.manet@neurochirurgie.fr)

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**Introduction:** The concept of external hydrocephalus refers to situations of CSF flow impairment within subarachnoid spaces (SAS). Classically described in infant and children, literature offers few data on adult.

**Material and methods:** We retrospectively analysed adult patients admitted in four French intensive care units, between November 2010 and December 2014, for severe traumatic brain injury (TBI) or subarachnoid hemorrhage (SAH). We undertook clinical and radiological findings of patients presenting intracranial hypertension (ICHT) presumably in relation with external hydrocephalus (delayed ICHT concomitant to a paradoxical enlargement of subarachnoid spaces), treated with cerebrospinal fluid (CSF) external lumbar drainage (ELD).

**Results:** 33 patients (19 men, mean age 46.7 yrs [+/-17.5]) admitted for TBI (n=22), SAH (n=8) or other brain insults (n=3) with a mean initial Glasgow score of 8 (+/- 4) were included. 25 (75.8%) patients did not receive former external ventricular drainage. In all cases, ELD was dramatically effective to lower intracranial pressure (25.2 mmHg [+/-9.1] before EDL vs 7.4 mmHg [+/-6.0] after EDL). No mydriasis or intracranial

bleeding occurred. One patient (3%) developed an ELD infection. Patients were discharged from ICU with a mean modified Rankin Score of 4[+/-1]. **Conclusions:** Often described as a passive process (e.g. hygroma), CSF accumulation around the brain after acute cerebral insults in adults can be approached as an active process of external hydrocephalus. This diagnosis remains often subtle, but should systematically be evoked when CT scan show paradoxical enlargement of subarachnoid spaces in a context of ICHT. Our data tend to confirm that in these specific situations, ELD should be considered as a safe, effective and minimal invasive option.

### P32

#### Ambulatory intracranial pressure monitoring in NPH with a miniaturized acquisition chain

Romain Manet<sup>1\*</sup>, Laurent Gergele<sup>2</sup>

<sup>1</sup>Department of Neurosurgery, University hospital of Saint-Etienne, France;

<sup>2</sup>Department of Intensive Care, University hospital of Saint-Etienne, France

E-mail: romain.manet@neurochirurgie.fr

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**Introduction:** Diagnosis of cerebrospinal fluid (CSF) disorders may require intracranial pressure (ICP) monitoring. Classically, recordings are performed with a cumbersome acquisition chain, requiring the patient to be bedridden in a specific environment. New solutions have recently been proposed to free patient of these constraints, by mean of telemetric technology. We report our first experience of the use of a miniaturized ambulatory acquisition chain.

**Material and methods:** Case report.

**Results:** We report the case of a 78yrs patient, suspected of normal pressure hydrocephalus (NPH), with non-contributive infusion test. ICP has been recorded during 36hrs, combining miniaturized elements of a classical acquisition chain. Thanks to its compact size, the device allowed patient to be free to have normal activity during the recordings, in particular to stand and walk out of the ward. Like with telemetric systems, ambulatory ICP monitoring is more realistic than bed monitoring. In this first case, monitoring did not show rise of ICP at any moment or any position, eliminating diagnosis of NPH. However, recordings confirmed the negativity of ICP in standing position, as reported in other publications using telemetric systems.

**Conclusions:** Recent publications concerning telemetric system of ICP recording are encouraging. However, reported morbidity (in particular infection rates) remains significantly higher than with classic ICP recording technics. In this reported case, we use a conventional ICP probe, with classical surgical technique. The large experience of intensive care confirmed the safety and the very low morbidity (in particular infectious risk) of classical ICP monitoring. Combining advantage of both methods (reduced bulk, low morbidity), miniaturized device could represent an interesting option for ambulatory ICP monitoring.

### P33

#### MRI Visualization of CSF Flow

Edward Frederick Melamed<sup>1\*</sup>, Skorn Ponartana<sup>2</sup>, Eisha Anne Christian<sup>3</sup>,

Matthew Borzage<sup>2</sup>, Stefan Bluml<sup>2</sup>, J Gordon McComb<sup>1</sup>

<sup>1</sup>Division of Neurosurgery, Children's Hospital Los Angeles, CA, USA;

<sup>2</sup>Department of Radiology, Children's Hospital Los Angeles, CA, USA;

<sup>3</sup>Department of Neurological Surgery, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

E-mail: emelamed@chla.usc.edu

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**Introduction:** The ability to non-invasively establish patency of cerebral spinal fluid (CSF) flow between adjacent central nervous system (CNS) compartments is of importance in the diagnosis and treatment of patients with various areas of CSF flow obstruction. Recent advances in magnetic resonance imaging (MRI) technology allows for real-time magnetic labeling of CSF to directly visualize flow through different compartments.

**Methods:** The presence of CSF flow was examined at the aqueduct of Sylvius (AS), the foramen of Monro (FM), the floor of the third ventricle (3rd V), and the foramen magnum (FMag) using a modification of arterial

**Table 1(abstract P33)**

	FM	3rd	V	FMag
Positive-True	26/26	8/8	12/12	30/30
False	0/26	0/8	0/12	0/30
Negative-True	16/25	0/2	2/3	1/3
False	9/25	2/2	1/3	2/3
Specificity	100%	0%	100%	100%
Sensitivity	74%	80%	92%	94%
Negative	LR 0.26	Undefined	0.08	0.06

spin labeling (ASL). The studies were compared with clinical information and classified as true positive, true negative, false positive, and false negative based on expectation of patency.

**Results:** A total of 68 flow studies were done on 44 patients. High correlation with true positive was seen at all four sites. No flow was visualized in 25 readings of the AS; in 9 of those cases we expected flow to be present. Table 1.

**Conclusion:** Establishing qualitative patency between adjacent CSF compartments using MRI is possible with a modified ASL technique. This technique has excellent (above 80%) sensitivity, specificity, and negative likelihood ratio in three out of the four regions studied.

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### P34

#### Patient age as risk factor for revision of ventriculopleural shunt

Edward Frederick Melamed<sup>1\*</sup>, Parham Yashar<sup>2</sup>, Eisha Anne Christian<sup>2</sup>, Cherisse Berry<sup>1</sup>, J Gordon McComb<sup>1</sup>

<sup>1</sup>Division of Neurosurgery, Children's Hospital Los Angeles, CA, USA;

<sup>2</sup>Department of Neurosurgery, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

E-mail: emelamed@chla.usc.edu

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**Introduction:** Ventriculoperitoneal shunts remain the standard of care for the treatment of hydrocephalus. However, for patients at risk of abdominal infection (e.g. following appendiceal rupture), those with a recent history of multiple abdominal surgeries, or for those who experience persistent symptoms due to inadequate absorption and possible pseudocyst, the ventriculopleural shunt (VPL) is a viable alternative.

**Methods:** We identified pediatric patients who underwent their initial VPL insertion at our institution from 1977-2013. Data was collected retrospectively from the clinical charts.

**Results:** 131 (78 M) patients were identified. Mean age at insertion of ventriculopleural shunt was 14 ± 5 years. Follow up was available on 124 patients with a mean duration of 50 months (range 0.1-288). Prior to and including VPL insertion, 58 patients with available preoperative data had experienced a mean of 3 ± 3 revisions. These patients underwent a mean of 1 ± 1 subsequent revisions of their VPL, significantly fewer than those of their prior shunt (p < 0.01).

At sixteen months post VPL insertion, half of the 102 patients with at least one year of follow up had undergone a shunt reoperation, either a revision or conversion to another shunt. 18/34 patients (53%) between twelve to sixteen-years-of-age and 21/39 (46%) patients aged seventeen or older required at least one subsequent VPL change in contrast to 23/29 (79%) patients under twelve-years-old at the time of insertion (p < 0.05). Kaplan Meir survival curves for the three age groups deviated significantly (p = 0.01). Furthermore, the hazard ratio of undergoing a shunt reoperation for patients under twelve was 1.9 (95% CI 1.2, 3.0) in comparison to either of the two older patient groups.

**Conclusion:** The ventriculopleural shunt is a viable alternative for patients who cannot tolerate a VP shunt or experience persistent

symptoms. After insertion these patients may be less likely to require additional revisions. The patient's age should be among the factors surgeons weigh carefully prior to VPL insertion. In comparison to older adolescents, children under twelve who undergo conversion to VPL may be at greater risk for subsequent shunt revision.

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### P35

#### Delayed management of secondary normal pressure hydrocephalus after cerebrospinal fluid external drainage

Vincent Meyer-Bisch<sup>1</sup>, Laurent Gergele<sup>2</sup>, François Vassal<sup>1</sup>, Benjamin Pommier<sup>1</sup>, Christian Auboyer<sup>2</sup>, Jérôme Morel<sup>2</sup>, Romain Manet<sup>1\*</sup>

<sup>1</sup>Department of Neurosurgery, University hospital of Saint-Etienne, France;

<sup>2</sup>Department of Anesthesiology and Intensive Care, University Hospital of Saint-Etienne, France

E-mail: romain.manet@neurochirurgie.fr

*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:P35

**Introduction:** External drainage (ED) of cerebrospinal fluid (CSF) is often used during management of brain insult. In absence of robust data and consensual guidelines, weaning ED remains challenging. The objective of the study was to assess the proportion of secondary normal pressure hydrocephalus (NPH), being treated with delay after ED weaning and to evaluate the resulting morbidity.

**Methods:** All adult patients admitted in intensive care unit for brain insult between 1st january 2010 and 31st december 2013, managed with ED, were included in this retrospective monocentric observational study. Rate and delay of shunt surgery after ED weaning were analysed in the light of neurological prognostic assessed by modified Rankin scale (mRS). Literature review. National numeric survey addressed by email in all french neurosurgical center.

**Results:** Among the 144 patients (57.6% of men) studied, 39% of the survivors developed a secondary NPH. Among them, 62, 5% were shunted early (from day 1 to day 7 after ED weaning) and 37.5% were treated with a delay (from 8 to 420 days after ED weaning). Identified risk factors of failure of the weaning test were: severity of initial neurological status (Glasgow score 9.5 vs 11), long delay between insult and ED insertion (226hrs vs 67hrs), low CSF outflow through ED (137mL/24h vs 194 mL/24h), high mRS at the moment of ED weaning (5 vs 4). Mean benefit of shunt insertion was 1 point of mRS in this population. Literature review found no evidence based data or guidelines to wean ED. National survey confirm the heterogeneity of ED weaning management.

**Conclusions:** This study confirms the imprecision of ED weaning in absence of guidelines and robust data, resulting in delayed management of secondary NPH in more than one in three patients. Methods of ED weaning should be more studied and probably up-graded.

### P36

#### The new proGAV 2.0 - a valve development based on systematical market observation

Christoph Miethke\*, Thoralf Knitter

Christoph Miethke GmbH & Co KG, Germany

E-mail: ceo@miethke.com

*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:P36

The treatment of hydrocephalus has been dramatically influenced by technical achievements which have been developed by different companies. One aspect was the principle phenomenological function of the device with the aim to lower the likelihood of negative complications like under- or overdrainage. Beneath these approaches it is important to observe the performance of the different devices based on intensive communication with the user. The manufacturer is not only obligated by law to systematically collect data about the performance of the devices. It is also important for significant improvement of the product.

Based on findings followed by systematical analyzes of revised valves, which have been send back to the manufacturer for investigation the

proGAV 2.0 has been developed to address nearly all critical points, which can be recognized during the investigations. Whereas the principle hydraulic function is nearly unchanged versus the first generation proGAV the handling, the risk of blockage, the risk of damaging the valve, the way of adjusting the valve as well as the verification of the setting have been improved and the basic technical elements have been completely reworked. The first clinical experiences support the intention of the approach as well as the information gained by returned valves.

The systematical observation of the performance of medical devices offers valuable information for improvements.

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### P37

#### The pattern of craniofacial encephalocel in Bethel Teaching General Hospital, Addis Ababa, Ethiopia

Tesfaye Mulat

Bethel Teaching general Hospital, Ethiopia

E-mail: tesfayeml@hotmail.com

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Craniofacial encephaloceles are commonly seen birth defects. The incidence is 1 in every 100, 000 live births. Six patients with craniofacial encephaloceles are treated by a combined craniofacial approach. The corrective measure allows reduction of the herniated encephalocele and correction of the craniofacial deformity in the same operation procedure. All cases admitted from May 2013 until June 13, 2014 to Bethel Teaching General Hospital were identified, and data were collected retrospectively, including demographics, clinical events, MRI and or CT scan findings, surgical techniques, complications and outcomes were analyzed using SPSS.

**Results:** See table 1.

The MRI finding in four of these patients shows only encephalocele, no hydrocephalus. In two of the cases beside the encephalocel, there is mild hydrocephalus. They need a follow up in six months. Four of the patients weight are below the standard.

All patients were doing well post operatively, no infections, bleeding or other complications.

**Discussions:** The surgery performed for all patients were frontal craniotomy including orbital roof was taken. Then encephalocele excision done both from facial and cranial side, followed by correction of the hypertelorism and nasal reconstruction. The surgery takes 5 to 7 hrs. The blood loss was replaces especially for the children below the age of 6. Post operatively they stayed in intensive care unit for two days, thereafter the edema started to decreased, in a week time they were discharged.

Four of the patients were from Oromiya region, the reason is that they were brought by NGO who are working in that region.

**Conclusion:** Even though craniofacial encephalocel seems rare in Western countries, it is not rare in this country. One of the reasons could be due to lack of Vit. B during pregnancy. This vitamin is essential for timely closure of the cranial bones. All of these patients are coming from the rural Ethiopia in very low socioeconomic where there is no antenatal care, most of the patients are malnourished. If we provide Vit. B during pregnancy we may reduce the incidence of this pathology.

**Consent to publish:** Written informed consent for publication of their clinical details was obtained from the patient/parent/guardian/relative of the patient.

**Table 1(abstract P37)**

Age	Sex	Origin	MRI	Outcome
5	M	Amahara (wollo)	No Hydrocephalus	Good
10	M	Oromiya (Harar)	Mild Hydrocephalus	Good
5	M	Oromiya (Nazerat)	Mild Hydrocephalus	Good
1.5	M	Oromiya (Harar)	No Hydrocephalus	Good
14	M	Oromiya (Harar)	No Hydrocephalus	Good
18	M	Oromiya (harar)	No Hydrocephalus	Good

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## P38

### Bradykinesia in idiopathic normal pressure hydrocephalus evaluated by quantitative finger tapping test: preliminary study

Namiko Nishida<sup>1\*</sup>, Yuko Sano<sup>2</sup>, Akihiko Kandori<sup>2</sup>, Hiroki Toda<sup>1</sup>, Sadayuki Matsumoto<sup>3</sup>, Koichi Iwasaki<sup>1</sup>, Masatsune Ishikawa<sup>4</sup>

<sup>1</sup>Department of Neurosurgery, Tazuke Kofukai Foundation, Medical Research Institute and Kitano Hospital, Japan; <sup>2</sup>Hitachi Ltd. Research & Development Group, Center for Technology Innovation - Healthcare, Japan; <sup>3</sup>Department of Neurology, Tazuke Kofukai Foundation, Medical Research Institute and Kitano Hospital, Japan; <sup>4</sup>Department of neurosurgery and normal pressure hydrocephalus center, Rakuwakai Otowa Hospital, Japan  
E-mail: n-nishida@kitano-hp.or.jp

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**Introduction:** Movement disorders in idiopathic normal pressure hydrocephalus (iNPH) are represented by gait disturbance (i.e., lower body bradykinesia). However, upper extremity bradykinesia was frequently found among iNPH patients. We assessed their upper extremity function by quantitative finger tapping test and checked the correlation with other demographic factors.

**Methods:** We evaluated the 10-second finger tapping movements of 8 patients (age: 78.4 ± 3.8 y; males: 5, females: 3) using magnetic-sensor coil system. Clinical symptoms were evaluated by the iNPH grading scale, minimal state examination and frontal assessment battery (FAB). The correlation of tapping parameters with clinical indicators was estimated.

**Results:** The patient's age correlated significantly with 6 of 21 finger-tapping parameters, including total tapping distance (Spearman  $r = -0.82$ ,  $p = 0.013$ ), coefficient of variation of maximum amplitude ( $r = -0.78$ ,  $p = 0.023$ ), energy balance ( $r = -0.72$ ,  $p = 0.046$ ), average maximum opening acceleration ( $r = -0.75$ ,  $p = 0.034$ ), tapping frequency ( $r = -0.85$ ,  $p = 0.005$ ), and average finger tapping interval ( $r = 0.87$ ,  $p = 0.007$ ). The severity of illness represented by iNPH grading scale correlated with other 2 parameters, including average maximum closing velocity ( $r = -0.73$ ,  $p = 0.043$ ) and coefficient of variation of maximum closing velocity ( $r = -0.79$ ,  $p = 0.047$ ).

**Conclusions:** Our data support the diagnostic value of quantitative finger tapping test for estimating the severity of bradykinesia underlying the iNPH symptomatology. Though preliminary, different patterns of correlations found in this study could potentially indicate the fundamental processes discriminating aging and disease progression.

## P39

### Relationship between flexion of the neck and changes in intracranial pressure

Sarah Skovlunde Hornshoej Pedersen\*, Morten Andresen, Alexander Lilja Jørgensen, Dorte Harpsøe Christoffersen, Marianne Juhler  
CSF Copenhagen Studygroup, Denmark  
E-mail: sarahshpedersen@gmail.com

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**Introduction:** Intracranial pressure (ICP) monitoring at our department includes a standardized postural change examination to evaluate its effects on ICP. During these procedures we observed that neck flexion caused an increase in ICP in one patient. To clarify if the observation was a random occurrence or if it could be reproduced, we added neck flexion and extension to the standard examination.

**Methods:** All patients undergoing invasive ICP monitoring at our department were included prospectively. The postural change examination consists of eight standard postures including both horizontal and vertical positions. In this abstract we focus specifically on the effect of neck flexion on ICP in the vertical positions. We examined the effect on ICP with the

patient sitting upright with a straight back and 1) a straight neck or 2) maximal neck flexion, and the patient sitting bent in "lumbar puncture position" with 3) neck flexion or 4) a straight neck. Each posture was maintained for ten minutes. We recorded ICP and demographic data.

**Results:** All 45 patients completed both measurements in the upright sitting position (18 male), while 38/45 patients also completed both measurements in "lumbar puncture position" (16 male). In both positions, flexion of the neck caused an increase in ICP in all patients.

In the upright sitting position the median ICP with 1) a straight neck was -5 mmHg (range -28 to 8 mmHg) while the median ICP with 2) neck flexion was 3 mmHg (range -18 to 19 mmHg). The median increase in ICP when flexing the neck was 8.5 mmHg (range 2.4 to 18 mmHg). The increase was highly significant ( $p < 0.001$ ).

The median ICP in the lumbar puncture position was 13 mmHg (range -15 to 38 mmHg) and -2.7 mmHg (range -28 to 14 mmHg) for respectively 3) neck flexion and 4) a straight neck. The median increase was 15.89 mmHg (range 8 to 25.7 mmHg). This increase in ICP was likewise highly significant ( $p < 0.001$ ).

**Conclusion:** The results indicate that the position of the neck has a more important influence on ICP than previously presumed. We speculate that the increase in ICP is a result of either compression of the jugular veins or the vertebral canal.

Further investigation indicates that the jugular veins indeed are affected by the position of the neck. 10 patients undergoing invasive ICP monitoring and postural change examination have been examined by ultrasound (UL). Primary results shows compression of the jugular veins in response to neck flexion and a correlation with an increase in ICP.

## P40

### Arterial hypertension and type 2 diabetes are frequent in iNPH

Okko T Pyykkö<sup>1\*</sup>, Ossi Nerg<sup>2</sup>, Anne M Koivisto<sup>2,5</sup>, Tuomas Rauramaa<sup>3,4</sup>, Mikko Hiltunen<sup>5</sup>, Juha E Jääskeläinen<sup>1</sup>, Ville Leinonen<sup>1</sup>

<sup>1</sup>Neurosurgery of NeuroCenter, Kuopio University Hospital, Kuopio, Finland; <sup>2</sup>Neurology of NeuroCenter, Kuopio University Hospital, Kuopio, Finland; <sup>3</sup>Department of Pathology, Kuopio University Hospital, Kuopio, Finland; <sup>4</sup>Unit of Clinical Pathology and Forensic Medicine, Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland; <sup>5</sup>Unit of Neurology, Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland  
E-mail: okko.pyykko@gmail.com

*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:P40

**Introduction:** Association of hypertension and diabetes with idiopathic normal pressure hydrocephalus (iNPH) has been described earlier, however, the prognostic role of these comorbidities is unknown.

**Methods:** All available hospital records and causes of death were reviewed retrospectively from a cohort of 283 iNPH patients with a median follow-up of 5.6 years (range 0.04–19.9 years) from a defined population in Middle and Eastern Finland.

**Results:** A total of 148 patients (52.3%) were hypertensive and 65 patients (23.0%) diabetic. Both diseases were equally distributed among sexes, and no age differences were observed between groups. In addition, short-term shunt-response was similar with a total of 85.1% of the 269 shunted patients showing a positive response. Mortality between diabetic and non-diabetic patients was similar (58.5% vs. 48.6%,  $p = 0.16$ ), however, median survival time was significantly lower in patients with diabetes compared to non-diabetic iNPH patients (6.3 vs. 9.8 years, log rank test  $p < 0.001$ ). No statistically significant differences of mortality or survival time were observed in hypertensive vs. non-hypertensive patients. The most frequent cause of death among all groups was coronary heart disease.

**Conclusions:** Both hypertension and diabetes are common in iNPH. A comorbid type 2 diabetes is a significant risk factor for earlier death.

## P41

### Long term follow up after surgery for benign intracranial cysts in children

Katrin KM Rabiei\*, Roberto Doria Medina, Mats Högfeldt, Carsten Wikkelso, Magnus Tisell  
Hydrocephalus research unit, Institution of Neuroscience, Sahlgrenska Academy, Sweden  
E-mail: katrinrabiei@gmail.com

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Arachnoid cysts are cystic malformations in cerebrospinal axis found in both adults and children. While most arachnoid cysts are asymptomatic and usually go undetected, some cause symptoms and warrant surgical treatment. In this prospective study we aimed to describe the result of short- and long term follow up in children referred to our center with a cystic malformation.

**Methods:** 27 pediatric patients (13 f, 14m, mean age 9, 4 y) with de-novo cysts were consecutively included during a 5 year period. Reason for initial investigation was headache, seizures, endocrine dysfunction, macrocephaly, balance disturbance and/or dizziness, trauma, cognitive disturbance and syncope. 22 patients underwent surgical treatment after initial evaluation with either open- or endoscopic fenestration of the cyst wall. Cyst volume was measured pre- and postoperatively with OsiriX software. Short term follow up was conducted 3 months and long term follow up 8, 6 years (7-10, 5 y) postoperatively.

**Results:** 60% (13/22) of the patients were improved after the short term - and 82% (18/22) after the long term follow up considering at least one major complaint. Operated cysts had a mean preoperative volume of 60 ml (5-225 ml) which postoperatively reduced with average of 56% at 3 month follow up. There was no significant difference in postoperative cyst volume between patients who improved and those who did not. Headache and imbalance improved significantly in the long-term follow up but not in the short term. Some individuals improved in Cognitive function, seizures and endocrine dysfunction. There was no permanent postoperative morbidity.

**Conclusion:** 82% of the children operated improved in the long-term follow up. Clinical improvement did not correlate with radiological improvement.

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1. Rabiei K, age 35 and Neurosurgical resident Sahlgrenska University Hospital, Sweden.

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#### P42

##### Diffusion tensor imaging in patients with idiopathic normal pressure hydrocephalus

Tomas Radovnický<sup>1\*</sup>, Daniel Adamek<sup>2</sup>, Milous Derner<sup>2</sup>, Martin Sames<sup>1</sup>

<sup>1</sup>Department of Neurosurgery, Masaryk Hospital, Usti nad Labem, Czech Republic; <sup>2</sup>Department of Radiology, Masaryk Hospital, Usti nad Labem, Czech Republic

E-mail: radovnicky@gmail.com

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**Introduction:** Idiopathic normal pressure hydrocephalus (iNPH) is well known as a treatable syndrome affecting an elderly people. There is a lack of specific radiological features, which can identify the iNPH patient. Diffusion tensor imaging (DTI) is a MRI technique for evaluation of the microstructural white matter characteristics, which can be affected by iNPH. Aim of this study was to find specific DTI sign for iNPH diagnosis.

**Methods:** This study was designed as a prospective, blinded, single institution study. We analysed MRI of 27 patients before the shunt surgery and 1 year after. DTI parameters (fractional anisotropy – FA, mean diffusivity – MD) were examined by 1, 5 T MRI in previously defined areas – the anterior and posterior limb of the internal capsule, the corpus callosum. iNPH patients were identified by clinical examination, dilatation of ventricles on MRI defined by Evans' ratio > 0, 30 and positive tap test and/or lumbar infusion test. Patient outcome was measured by iNPH grading scale one year after surgery. As a control group we examined 24 age-matched healthy controls. DTI values were statistically analysed.

**Results:** FA in the posterior limb of the internal capsule was significantly higher in iNPH patients compared to the healthy controls (0, 70 vs. 0, 58,  $p < 0, 05$ ).

The analysis of FA and MD values before and after the shunt surgery shows the significant decrease of FA in the posterior limb of the internal capsule (mean 0, 70 before and 0, 63 after the surgery,  $p < 0, 05$ ). But the postoperative FA in the posterior limb of the internal capsule was still higher than in the healthy control group. No significant change in other areas was identified.

In the group of 27 iNPH patients were 4 shunt non-responders (14, 8%). No significant difference between FA and MD values in responders and non-responders was found.

**Conclusions:** Fractional anisotropy value in the posterior limb of the internal capsule was significantly higher in iNPH patients compared to the healthy control group. This value significantly decreased after the surgery. But it failed in the differentiation of patients with response to the shunt surgery from the non-responders. Higher FA in the posterior limb of the internal capsule is supportive for iNPH diagnosis, but it shouldn't be used as a single predictor.

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#### P43

##### Disproportionately enlarged subarachnoid space hydrocephalus presence in patients with idiopathic normal pressure hydrocephalus

Tomas Radovnický<sup>1\*</sup>, Daniel Adamek<sup>2</sup>, Milous Derner<sup>2</sup>, Martin Sames<sup>1</sup>

<sup>1</sup>Department of Neurosurgery, Masaryk Hospital, Usti nad Labem, Czech Republic; <sup>2</sup>Department of Radiology, Masaryk Hospital, Usti nad Labem, Czech Republic

E-mail: radovnicky@gmail.com

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**Introduction:** Idiopathic normal pressure hydrocephalus (iNPH) is a treatable disease of an elderly people. It's known for 50 years, but there are still some controversies, especially in the diagnostic algorithm. Disproportionately enlarged subarachnoid space hydrocephalus (DESH) seems to be important radiological feature of iNPH, but it's not present in all patients. The aim of our study was to analyse appearance of DESH in our set of patients.

**Methods:** We retrospectively analysed 1, 5 T MRI in 27 iNPH patients before surgery and MRI in 24 healthy controls. Evaluation was performed by neurosurgeon and radiologist independently and blindly. We assessed tight high convexity and medial subarachnoid space, dilatation of Sylvian fissure and focal dilatation of sulci. iNPH patients were identified by clinical examination, dilatation of ventricles on MRI defined by Evans' ratio > 0, 30 and positive tap test and/or lumbar infusion test. Patient outcome was measured by iNPH grading scale one year after surgery.

**Results:** In the group of 27 iNPH patients, we have found DESH presence in 15 cases (55, 6%), all 15 patients were shunt responders. In the group of 12 iNPH patients without DESH 4 of them did not respond to surgery (33, 3%).

Among the 24 healthy controls, we haven't found any DESH appearance.

**Conclusion:** We confirmed, that DESH appearance on MRI is supportive for the iNPH diagnosis, but it should not be used as a single predictor. Patients without DESH are at a higher risk to be shunt non-responders. Indication for shunt surgery should be still based on correlation between the radiological and clinical evaluation and supplementary CSF dynamics tests.

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#### P44

##### A generalization of the Marmarou model

Kaylan Raman

Northwestern University, USA

E-mail: kalyraman@gmail.com

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**Introduction:** The Marmarou model has fundamentally influenced the development of mathematical pressure-volume models of cerebrospinal fluid (CSF) dynamics. It is a non-linear ordinary differential equation which is solvable in closed-form. The solution provides valuable analytical insights into the nature of the circulatory dynamics of CSF. It would be useful to generalize the Marmarou model to a broader class of polynomials to expand its scope to other CSF and Hydrocephalus phenomena.

**Methods:** The Marmarou model relating the temporal evolution of ICP in pressure-volume studies to infusions incorporates observed fluctuations in the ICP through a nonlinear ordinary differential equation (ODE) of second order whose structure is based on physical analogies between CSF dynamics and an electrical circuit. This ODE is extended from its quadratic structure to a general polynomial of order 'n'.



**Results:** An algorithm to solve the general polynomial ODE is developed. The solution to the original Marmarou model emerges from this algorithm as a special case. The solution for the general polynomial ODE is obtained from the algorithm which is shown to be easily implementable.

**Conclusions:** The general polynomial Marmarou model expands the domain of applicability of the original one, thereby providing insights into a broader class of CSF phenomena. From a clinical perspective, these insights have implications for risk management of the patient for a large class of CSF and Hydrocephalus phenomena.

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#### P45

##### The shunt from hell: management based on the point of obstruction

Harold L ReKate

Hofstra Northshore LJ School of Medicine, United States of America

E-mail: Haroldrekate@gmail.com

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**Introduction:** After two years of study and conversation a group of 20 hydrocephalus investigators developed a consensus on a new classification of hydrocephalus based on point of obstruction. This new classification has proved useful in the diagnosis and treatment of patients with hydrocephalus of all types and is especially helpful in assessing the various treatment options for the individual patient.

**Methods:** This is a retrospective review of a patient with a complex form of hydrocephalus related to a Dandy Walker Malformation who had had over 60 shunt revisions in the two years prior to first being seen at our institution. She was evaluated as to potential points of obstruction and the best treatment for each point. The plan was to make certain that all compartments containing CSF were to be made to communicate with each other and that a maximum of one valve would be used if further treatment is needed.

**Results:** Using injections of Iohexal tracer for CT it was shown that there were very small lateral and third ventricles and obstruction to flow from through the aqueduct and from the cortical subarachnoid space into the encysted fourth ventricle. Treatment progressed in stages with fenestration of the cyst and replacing the shunt with a reservoir and "Butterfly needle." The lateral and third ventricle dilated and it was shown that now there was a fourth ventricle containing a floppy collapsed cyst within it. Following endoscopic third ventriculostomy she is now without a shunt and is back to school for the first time in 2 years. Follow up is 9 months.

**Discussion:** The vast majority of cases of hydrocephalus are due to distinct sites of obstruction to flow of CSF. Normal CSF dynamics demand that all CSF compartments communicate freely and that the intracranial pressures are normal. At this point if the ventricles are able to increase in size the patient is likely (>80%) to be able to be managed without a shunt with or without an endoscopic third ventriculostomy.

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#### P46

##### Cerebral venous sinus stent insertion as a primary versus secondary procedure in the treatment of intracranial hypertension

Syed N Shah<sup>\*</sup>, Aswin Chari, Simon D Thompson, Patricia Haylock-Vize, Jinendra Ekanayake, Edward W Dyson, Andrew R Stevens, Claudia Craven, Huan W Chan, Tarek Mostafa, Neeikhil A Patel, Samir A Matloob, Ahmed K Toma, Laurence D Watkins

National Hospital for Neurology and Neurosurgery (NHNN), UCLH, UK

E-mail: syed.shah9@live.co.uk

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**Introduction:** Venous sinus stent insertion is being increasingly used as a primary treatment for intracranial hypertension patients (BIH). However,

the value of this treatment modality is still controversial. This study looks into the difference in effectiveness of stents inserted as a primary procedure and those inserted in patients who already had cerebrospinal fluid diverting shunt in place i.e. as a secondary procedure.

**Materials and methods:** A retrospective case series of patients with intracranial hypertension treated in our unit with venous sinus stent insertion. Case notes were reviewed for clinical presentation, initial response to stent insertion and follow up results. Patients in group A did not have previous shunt before insertion of stent (stent as primary procedure) while group B patients already had shunt(s) in situ (stent as secondary procedure). Stent survival time was defined as number of days from stent insertion until the next intervention due to worsening/recurrent symptoms or end of follow up period (June 2015).

**Results:** In total, 44 patients underwent stent insertion between 2011 and 2015 (24 patients in group A and 20 in group B). Follow-up period was 490 ± 453 days (mean ± standard deviation); group A 548 ± 522 days and group B 420 ± 488 days (p=0.6). The stent survival time in group A was 435 ± 453 days compared with group B: 270.95 ± 394.86 days (p= 0.03). A total of 13 patients required further surgical intervention during the follow up period, of which 4 (16%) were in group A and 9 (45%) in group B (p=0.001).

**Discussion:** The results suggest that stent insertion is a relatively effective method of treatment of patients with intracranial hypertension. Lower survival rates of stents inserted as a secondary procedure could be related to the fact that shunts change the cerebrospinal fluid hydrodynamics interfering with stent function or simply due to the fact that group B patients have more aggressive form of intracranial hypertension.

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#### P47

##### Prompt neuroendoscopic intervention prevented hydrocephalus after ventricular rupture of the brain abscess. A case report

Toshimasa Shin<sup>\*</sup>, Hisayuki Murai, Hirokazu Sunaoka, Naokatu Saeki

Chiba University Graduate School of Medicine, Japan

E-mail: toshi826@hotmail.co.jp

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**Introduction:** Ventricular abscess is one of the worst complications of the brain abscess. Despite standard treatments such as continuous ventricular drainage and antibiotic agents, ventricular abscess frequently causes hydrocephalus or isolated ventricles. And its morbidity and mortality is high. In the present article, a case of brain abscess with intraventricular rupture successfully treated with prompt neuroendoscopic ventricular lavage is reported.

**Case presentation:** An eleven years old male was admitted to our hospital with headache and fever. Magnetic resonance imaging (MRI) showed right frontal and left parietal mass lesion. The right frontal mass lesion was 22 mm, and the left was 24mm in diameter. Diffusion weighted MRI showed high intensity areas in both lesion and frontal lesion was closely located to the lateral ventricle. Gadolinium contrast enhanced MRI showed ring enhancement of both lesions. Despite 4 days use of antibiotics, the volume of lesions expanded and ventricular abscess became evident on MRI. He became restless and confused, so we performed drainage of both abscess and ventricular lavage with flexible neurovideoscope (Olympus VEF-V). At a day after the operation, he became alert and calm. The lesions disappeared on MRI after 2 months and he was discharged. His chest computed tomography showed two pulmonary nodules of arteriovenous malformation (AVM) which was successfully embolized later.

**Conclusions:** We presented a case of successfully treated ventricular abscess with prompt ventricular lavage. It avoided hydrocephalus or ventricular shunt surgery. However this report is preliminary and we need more cases to confirm its efficacy and safety, prompt neuroendoscopic intervention to ventriculitis is seemed to be promising.

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#### P49

##### Calcium antagonism effects on cerebral blood flow in rats with acute hydrocephalus

Alexander Victor Shulyakov<sup>1,2\*</sup>, Richard J Buist<sup>3</sup>, Domenico L DiCurzio<sup>2,4</sup>, Marc Ronald Del Bigio<sup>1,2</sup>

<sup>1</sup>Department of Pathology University of Manitoba, Canada; <sup>2</sup>Manitoba Institute of Child Health, Winnipeg, Canada; <sup>3</sup>Department of Radiology,

Faculty of Medicine University of Manitoba, Canada; <sup>4</sup>Department of Human Anatomy & Cell Science University of Manitoba, Canada  
E-mail: ashulyakov@mich.ca  
*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:P49

**Introduction:** Calcium ion antagonism shows some benefit in experimental hydrocephalus, but the interrelationship between the cerebral vasculature, cerebral blood flow (CBF), and ventriculomegaly remains unclear.

**Methods:** Rats were injected with kaolin at 35 days and were studied after 12-15 days. CBF was measured with and without nimodipine or magnesium sulfate using magnetic resonance and fluorescent microspheres. Arterial blood and intracranial pressure (ICP), acid-base, oxygen/hemoglobin, and electrolytes status was measured. Intraparenchymal vascular remodeling was also determined in brains of hydrocephalic rats treated with calcium antagonists for 2 weeks.

**Results:** Increased ICP did not significantly affect cerebral perfusion pressure within the range of normal autoregulation. CBF significantly decreased in acutely hydrocephalic rats. Nimodipine and magnesium sulfate decreased systemic arterial blood pressure, cerebral perfusion and intracerebral pulse pressure; however, there was no change in cerebral blood flow. There was no change in white matter vascular density after 2 weeks treatment.

**Conclusions:** Cerebral hypoperfusion occurs in acute experimental hydrocephalus, however the calcium channel antagonists nimodipine and magnesium sulfate, do not increase the CBF. Reduced intracranial pulse pressure possibly mitigates development of acute hydrocephalus.

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#### P50

##### Paradoxical supine overdrainage with ventriculoatrial shunt

David Solomon<sup>1</sup>, Abhay Moghekar, Ari Blitz  
Johns Hopkins University, USA  
E-mail: dsolomo4@jhmi.edu  
*Fluids and Barriers of the CNS* 2015, **12(Suppl 1)**:P50

**Introduction:** Antisiphoning devices and gravitational valves (ShuntAssistant) have been used successfully to decrease overdrainage of CSF due to postural change, by limiting the amount of CSF outflow in the upright position. The possible advantage of a VA configuration conferred by a smaller hydrostatic column is lessened by the lack of a longer, smaller diameter distal catheter. We observed subatmospheric intracranial pressure in supine patients with ventriculoatrial shunt, associated with headaches that were worse lying down and upon awakening in the morning.

**Methods:** Patients in this case series had ventriculoatrial shunting for pseudotumor cerebri, with a ShuntAssistant in series with a programmable differential valve. Intracranial pressure was determined by measuring CSF pressure through a lumbar spinal catheter with the fluid-coupled transducer at the level of the external auditory meatus, after zeroing to atmospheric pressure. Respiration was measured with impedance plethysmography. Data were continuously sampled at 100 Hz and stored for offline analysis.

**Results:** CSF pressure gradually decreased to below zero when patients' position changed from upright to lying down. Supine pressures were often lower than when patients were sitting upright, opposite to the usual situation in both shunted and physiologic conditions. Mean CSF pressure could be between -5 and -10 mm Hg for hours, with the amplitude of respiratory modulation of the ICP waveform as great as 15 mm Hg. Contrast-enhanced brain MRI did not show pachymeningeal enhancement or dural thickening, but often showed asymmetric ventricles consistent with overdrainage.

**Conclusions:** The usual mechanism for ventricular shunt overdrainage – hydrostatic pressure due to fluid in the distal catheter – cannot explain these observations. Negative inspiratory intrathoracic pressure associated with obstructed breathing is a likely cause, given the large respiratory modulation of the pressure waveform. Aspiration due to blood flow around the distal catheter tip is an additional possible mechanism, especially since there is increased venous return to the heart during inspiration. We suggest that negative ICP in the supine patient is due to a respiration-generated pressure gradient favoring venous outflow through the cerebral sinuses, and CSF outflow through the differential valve, with no added resistance from the additional gravitational valve.

Headaches worse when lying and present upon awakening in the morning may be mistakenly attributed to elevated ICP, prompting adjustment to a lower valve opening pressure. When patients with VA shunt have labored breathing and some degree of ventricular collapse, abnormally low ICP due to paradoxical supine overdrainage should be considered.

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#### P51

##### NPH: are we giving up on patients with temporary improvement post shunt?

Simon Thompson<sup>\*</sup>, Claudia Craven, Patricia Haylock-Vize, Edward Dyson, Aswin Chari, Samir Matloob, Neekhil Patel, Syed Shah, Andrew Stevens, Huan Wee Chan, Jinendra Ekanayake, Ahmed Toma, Lewis Thorne, Laurence Watkins  
The National Hospital for Neurology and Neurosurgery, UK  
E-mail: simon.thompson3@nhs.net  
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**Introduction:** Normal pressure Hydrocephalus (NPH) is predominantly treated with a ventriculoperitoneal shunt (VPS) resulting in improvement in the Hakim triad (mobility, cognitive function, urinary continence). There are a population of patients who experience an improvement in symptoms post shunt insertion followed by a subsequent deterioration in their condition in the preceding months / years. At our institution, a large volume (min 40ml) CSF withdrawal is made via the shunt reservoir in these patients, measuring pre/post mobility and cognitive function. Comparison is then made between pre/post results and if a clear improvement is seen, VP shunt surgical revision is offered.

**Methods:** A single centre retrospective audit. Medical notes of temporarily improved NPH patients, admitted for a VPS Tap test and subsequent shunt revision at our institution over the past four years were reviewed. Walking test assessed over a 10m course at baseline, post initial shunt, pre Tap test, post tap test and post shunt revision were compared. Subjective feedback from patient / family also assessed.

**Results:** 29 patients underwent tap tests via VPS shunt reservoir. No cases of shunt infection or sub-dural collections experienced post tap. 19 patients showed clinical improvement post Tap, 2 unable to withdraw CSF and subsequently underwent proximal catheter revision, 8 did not see improvement post tap and did not proceed with further neurosurgical treatment. Of the 19 positive results, 18 subsequently underwent shunt revision and 1 was lost to follow-up. All patients saw an improvement in symptoms post shunt revision including patients who had a proximal catheter blockage. 16 patients underwent insertion of Miethke Pro-SA valve post revision and 2 underwent insertion of Miethke Pro-GAV valve.

**Conclusion:** Taping of VP shunt in NPH patients with suspected blocked / under functioning shunt is a safe procedure and shows an accurate predictive value for improvement post surgery.

## P52

### Elective ICP monitoring: how long is long enough?

Simon Thompson<sup>1\*</sup>, Hasan Asif<sup>2</sup>, Claudia Craven<sup>1</sup>, Patricia Haylock-Vize<sup>1</sup>, Edward Dyson<sup>1</sup>, Aswin Chari<sup>1</sup>, Samir Matloob<sup>1</sup>, Neekehil Patel<sup>1</sup>, Syed Shah<sup>1</sup>, Andrew Stevens<sup>1</sup>, Huan Wee Chan<sup>1</sup>, Jinendra Ekanayake<sup>1</sup>, Ahmed Toma<sup>1</sup>, Lewis Thorne<sup>1</sup>, Laurence Watkins<sup>1</sup>

<sup>1</sup>The National Hospital for Neurology and Neurosurgery, UK; <sup>2</sup>Imperial College London, UK

E-mail: simon.thompson3@nhs.net

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**Introduction:** Elective intracranial pressure (ICP) monitoring is a useful tool in the diagnosis and evaluation of simple and complex cerebrospinal fluid dynamic disturbances. Whilst many previous research papers have focused on patients undergoing ICP monitoring acutely following traumatic brain injury (TBI), few have looked into the duration of monitoring required to achieve an accurate picture of a patient's intracranial dynamics in non acute, elective cases. At our institution we currently complete monitoring for a period of >48hrs.

**Methods:** A retrospective audit, assessing any patient admitted electively to our institution for ICP monitoring over a 3 month period. Exclusion criteria included acute admissions and patients who underwent a change in their treatment whilst undergoing ICP monitoring (such as CSF shunt valve adjustment / surgical procedures and/or medication changes which could affect ICP i.e. Acetazolamide). ICP results were analysed focusing on median ICP and Median pulse amplitude over three time periods: total data collected v first 48hrs of data collection v first 24hrs of data collection.

**Results:** 18 patients met the desired criteria. Mean length of monitoring was 3 days (range 2-5) for the total number of patients. There was no significant difference between 24hrs and 48hrs duration of monitoring for the median ICP ( $p > 0.05$ ) and ICP pulse amplitude ( $p > 0.05$ ).

**Conclusion:** 24 hour monitoring of ICP in elective patients in a stable condition without changes to their current treatment is sufficient to detect mean ICP and pulse amplitude. Further studies may be appropriate to assess if fewer than 24hrs monitoring can also prove an accurate method of monitoring ICP.

## P53

### Distribution of amyloid burden is different between idiopathic normal pressure hydrocephalus and Alzheimer's disease

Takahiko Tokuda<sup>1\*</sup>, Masaki Kondo<sup>1</sup>, Nagato Kuriyama<sup>1</sup>, Shigenori Matsushima<sup>1</sup>, Hiroto Nakanishi<sup>2</sup>, Masatsune Ishikawa<sup>3</sup>

<sup>1</sup>Kyoto Prefectural University of Medicine, Japan; <sup>2</sup>Nishijin Hospital, Japan;

<sup>3</sup>Normal Pressure Hydrocephalus Center, Otowa Hospital, Japan

E-mail: ttokuda@koto.kpu-m.ac.jp

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**Introduction:** In patients with idiopathic normal pressure hydrocephalus (iNPH), one of the potential factors that may negatively influence the shunt responsiveness is the presence of comorbidity, especially the Alzheimer's disease (AD) that results in progressive dementia. It is hence essential to conduct an accurate diagnosis on whether each patient with iNPH has comorbid AD. Recently, positron emission tomography (PET) using 11C-labeled radiotracer Pittsburgh Compound B (PIB) has been widely applied for the in vivo assessment of amyloid- $\beta$  (A $\beta$ ) deposition in patients with AD. To elucidate the incidence and distribution of the cortical retention of Pittsburgh Compound B (PIB) in patients with iNPH and clarify the differences from those in patients with AD.

**Methods:** Ten patients with iNPH without any clinical signs indicative of AD were enrolled in this study. Cerebral retention of PIB in positron emission tomography (PET) in iNPH patients was compared with those in 7 age-matched AD patients. The CSF levels of  $\beta$ -amyloid 1-42 peptide (A $\beta$ 42), which inversely decrease with cerebral amyloid burden, were also measured.

**Results:** Three of the 10 patients with iNPH showed increased cortical PIB retention. Although the mean cortical SUV ratios were similar, the distribution of PIB retention was much different between the patients with iNPH and AD. The PIB retention was limited to the high-convexity

parasagittal areas in iNPH patients, while it spread over the frontal and parietotemporal areas in AD. The coronal images of PIB-PET were more informative than conventional transverse images in evaluating the distribution pattern of cortical PIB retention. Two iNPH patients with higher cortical PIB retention had the lowest levels of CSF A $\beta$ 42, indicating that PIB retention in iNPH would not reflect a simple delay in the clearance of PIB but its binding to real-existing A $\beta$  amyloid in the brain. **Conclusions:** Our results indicate that iNPH is one of the diseases that can exhibit cortical PIB retention. The characteristic distribution of PIB retention in iNPH could be useful in differential diagnosis between iNPH and AD.

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## P54

### Investigating hydrocephalus using Multiple-network Poroelectric Theory

John Christopher Vardakis<sup>1\*</sup>, BJ Tully<sup>2</sup>, L Guo<sup>1</sup>, Y Ventikos<sup>1</sup>, D Chou<sup>3</sup>

<sup>1</sup>University College London, United Kingdom; <sup>2</sup>First Light Fusion Ltd., UK;

<sup>3</sup>Institute of Biomedical Engineering and Department of Engineering Science, University of Oxford, Oxford, UK

E-mail: j.vardakis@ucl.ac.uk

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**Introduction:** The function of the brain depends on the transport of a multitude of fluids, namely blood, cerebrospinal fluid, interstitial fluid and intracellular fluid. Our ability model these intertwined fluid transport processes within brain tissue in an anatomically accurate and patient-specific manner is of ever-increasing significance, especially since integrative systems possess numerous interactions with the external world which either directly or indirectly affect brain function and homeostasis.

**Methods:** The current state of knowledge about hydrocephalus (HCP), and more broadly integrative cerebral dynamics and its associated constitutive requirements, advocates that poroelectric theory provides a suitable framework to better understand such a disease. Multiple-network Poroelectric Theory is used to develop a novel spatio-temporal model of tissue displacement and fluid regulation in varying scales within the cerebral environment. The system of equations is discretized in a variety of formats, and in all three spatial dimensions. Both obstructive (mild and severe aqueductal stenosis, 4th ventricle outlet obstruction) and communicating hydrocephalus was investigated in a variety of settings, and accompanied by surgical techniques such as Endoscopic Third and Fourth Ventriculostomy (ETV and EFV). Aquaporin-4 swelling characteristics have also been incorporated into this MPET through the use of simple, functional relationships.

**Results:** Ventriculomegaly, CSF/ISF pressure, wall shear stress and pressure difference between lateral and fourth ventricles increased with applied stenosis, and subsequently dropped to nominal levels with the application of ETV. The greatest reversal of the effects of atresia of the 4th ventricle comes by opting for ETV rather than the more complicated procedure of EFV. Periventricular swelling can also be observed at various stages of HCP development, in both obstructive and communicating HCP simulations.

**Conclusions:** This work presents an assessment of the impact of aqueductal stenosis and 4th ventricle outlet obstruction, along with the applications of ETV and EFV on an anatomically accurate representation of the cerebroventricular system. Theoretical adaptations to communicating HCP were also investigated. Evolution of the MPET model can lead to a level of complexity that could allow for an experimentally guided exploration of areas that would otherwise prove too intricate and intertwined under conventional settings.

## P55

### Automated calculation of brain parenchymal fraction as a fast and user-independent method to monitor intracranial CSF volume in hydrocephalus

Johan Virhammar<sup>1\*</sup>, Marcel Warntjes<sup>2,3</sup>, Katarina Laurell<sup>4</sup>, Elna-Marie Larsson<sup>5</sup>  
<sup>1</sup>Department of Neuroscience, Neurology, Uppsala University Hospital, Sweden; <sup>2</sup>Center for Medical Imaging Science and Visualization (CMIV), Linköping University, Linköping, Sweden; <sup>3</sup>SyntheticMR AB, Linköping, Sweden; <sup>4</sup>Department of Pharmacology and Clinical Neuroscience, Umeå University, Sweden; <sup>5</sup>Department of Surgical Sciences, Radiology, Uppsala University, Sweden

E-mail: johan.virhammar@gmail.com

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**Introduction:** Removal of a bolus of CSF by a lumbar puncture (tap test) can be used as a prognostic test in normal pressure hydrocephalus (NPH). The brain parenchymal fraction (BPF) is calculated as (intracranial volume – CSF volume) / intracranial volume. An automatic method to calculate BPF was compared with manual segmentation of lateral ventricular volume as methods to monitor changes in intracranial CSF after a tap test.

**Methods:** A lumbar puncture with drainage of 40 mL CSF was performed in 23 patients with idiopathic NPH. Magnetic resonance imaging (MRI) was performed with a 3T scanner with a sequence (QRAPMASTER) allowing quantification of relaxation times. MRI was done at two times before, and at 30 minutes, 4 hours and 24 hours after the tap test. At each investigation time, the volume of the lateral ventricles was manually segmented. BPF was automatically calculated using the post-processing software SyMRI 7.0 (Synthetic MR, Sweden). SyMRI simultaneously measures T1 and T2 relaxation and proton density (PD) values to segment intracranial volume (ICV), gray matter (GM), white matter (WM) and CSF. Summation of the tissues over the complete imaging volume automatically produces GM, WM and CSF volumes in less than 2 minutes.

**Results:** At 30 minutes after the lumbar puncture, the volume of the lateral ventricles decreased 5.6±1.9 mL ( $p<0.0001$ ) using manual segmentation while BPF increased 0.78±0.41% ( $p<0.001$ ). Differences were significant for both methods also at 4 hours and 24 hours after the tap test. There was a correlation between change in BPF and change in manually segmented ventricular volume with goodness of fit  $R^2=0.45$  ( $p<0.0001$ ).

**Conclusions:** BPF is provided rapidly and fully automatically with SyMRI and can be used to monitor changes in intracranial CSF volume. These changes correlate with changes of ventricular volume and may be used for the clinical monitoring of hydrocephalus.

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## P56

### The patent persistent fibrous tract in an adolescent person who presented with disconnected lumboperitoneal shunt: a case report

Kei Yamashiro<sup>1\*</sup>, Kiyoshi Takagi<sup>2</sup>, Yasuhiro Yamada<sup>1</sup>, Daisuke Suyama<sup>3</sup>, Tsukasa Kawase<sup>1</sup>, Yoko Kato<sup>1</sup>

<sup>1</sup>Fujita Health University Banbuntane Hotokukai-Hospital, Japan; <sup>2</sup>Chiba Kashiwa Tanaka Hospital, Japan; <sup>3</sup>Fuchu Keijinkai Hospita, Japan

E-mail: keiyamashiro1577@gmail.com

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**Introduction:** Disconnection of proximal or distal catheter is seen more frequently in the complication of the lumboperitoneal (LP) shunt. The

literatures didn't establish whether the disconnected LP shunt can be allow passage of cerebrospinal fluid (CSF) though the disconnected portion. We present a case of young patient with disconnected LP shunt who reported patent persistent fibrous tract around the tube shunt.

**Case illustration:** A 17-year-old man was performed LP shunt at 12 year-old due to pseudomeningocele from suboccipital decompression in the Arnold-Chiari type I malformation. LP shunt revision was performed 8 months after because of shunt malfunction. However, he complained about low back pain after revision. Radiographic studies demonstrated the proximal catheter disconnected and CSF couldn't aspirate from the flushing device. The LP shunt removal was performed and subcutaneous mass from CSF collection was observed after the closing of proximal fibrous tract by tabasco-bag suture. The patient complained about severe headache after the procedure. The lumbar puncture revealed the high pressure of 40 cmH<sub>2</sub>O. The LP shunt emergency was done then the patient turned to dramatically disappear of severe headache.

**Conclusions:** Even if the shuntography cannot be performed, the clinical course can be strongly indicated that the fibrous tract remained patent after the shunt has been proved for disconnection. LP shunt operation is popular for hydrocephalus treatment and the proximal catheter disconnection is frequently found. A shuntography can identify functioning of shunt and guide management, we should perform shuntography before removal of the shunt.

## P57

### The quantitative motion analysis using portable gait rhythmogram after CSF drainage in the patients with idiopathic normal pressure hydrocephalus

Makiko Yogo<sup>\*</sup>, Shusaku Omoto, Masayo Morita, Masahiko Suzuki  
Department of Neurology, The Jikei University School of Medicine, Katsushika Medical Center, Tokyo, Japan

E-mail: makiko.yogo@gmail.com

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**Introduction:** We previously reported that portable gait rhythmogram (PGR) equipped with accelerometers to identify gait-induced accelerations enable us to quantitative gait analysis in Parkinson's disease (PD). We objected to reveal the quantitative gait differences between idiopathic normal pressure hydrocephalus (iNPH), PD and normal controls (NC) using PGR.

**Methods:** The study subjects were 7 patients with iNPH (age 76.9±2.6 years, 6 men and 1 woman), 12 patients with de novo PD who were not medicated with any kinds of anti-parkinsonian drug (age 68.3±4.5 years, 5 men and 7 women, 2 patients with Hoehn and Yahr stage I, 2 with stage II, 8 with stage III. The duration of illness was 2.3±1.6 years.) We also studied 17 NC (age 64.7±4.5 years, 8 men and 9 women).

24hours continuous recordings were performed twice before and after CSF drainage in iNPH patients with a trunk-mounted PGR. In PD and NC, 24hours continuous recordings were performed once at arbitrary point.

We calculated the "amount of overall movements per 24 hrs" from all motion-induced acceleration as an index of hypokinesia, "gait cycle and cadence" from the gait signals as indexes of step length, and "gait acceleration range" as an index of step power.

**Results:** Comparing with NC and PD, the average data obtained from 6 CSF drainage responded iNPH patients showed lower "amount of overall movements per 24 hrs". Faster "gait cycle" and higher "cadence" which indicate narrower step lengths, and lower "gait acceleration range" which indicate ineffective floor reaction forces in iNPH patients were also detected. Improvements in gait following spinal CSF drainage were observed using PGR.

In representative case of CSF drainage responded patients, gait defects improved after CSF drainage, and the improvement lasted after LP shunt was performed. Same tendency were observed in the average result of responded patients, though it was not statistical significant.

Whereas, no alteration was observed after CSF drainage in an unresponded subject.

When considering percent changes of parameters, positive correlations were found between "amount of overall movements" and points of FAB, between "cadence" and points of MMSE, between "cadence" and 10m walk time. Negative correlation was found in "amount of overall

movements" and 10m walk time, between "gait acceleration range" and points of FAB.

**Conclusions:** PGR revealed narrower and more monotonous step length in iNPH patients than PD and NC. And it also detected gait improvements following CSF drainage in the CSF drainage responded patients. Thus, PGR can analyze long durational gait in daily life and provide additional quantitative data on former measurements of CSF drainage easily and usefully.

## P58

### The treatment of endoscopic third ventriculostomy for hydrocephalus caused by tectal plate gliomas

Jiaping Zheng\*, Guoqiang Chen, Qing Xiao

Aviation General Hospital of China medical university, China, People's Republic of

E-mail: redleo@sina.com

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**Objective:** Because of the characteristic of the anatomical location, it is easy for the tectal plate gliomas to cause obstructive hydrocephalus. Endoscopic third ventriculostomy is used for the treatment of obstructive hydrocephalus caused by tectal plate gliomas of the children. Evaluate the prognosis of patients with postoperative follow-up.

**Methods:** Preoperative MRI prompted that there were tegmental region masses in 13 children with hydrocephalus. The increase was not obvious. The fiber neuroendoscopy was used for the endoscopic third ventriculostomy. During the operative observation of mesencephalon tegmental region, the hyperplasia of periaqueductal nerve tissue with light pink rough surface and the occlusive aqueduct opening could be observed.

**Results:** Followed up for 1-8 years, the average follow-up is 3.6 years. After the operation, 13 patients with the symptoms of headache and unclear vision were in remission and the ventricle was decreased. Postoperative symptom was not in remission in two cases of patients with preoperative diplopia. The treatment of gamma knife was used in one case of patient. The patient was died of radiation encephalopathy after 1 year. Six months after the operation, the symptom of diplopia appeared in 1 case of patient. Reexamination of magnetic resonance imaging (MRI) showed that the tumor increased. 6 months after tumor resection, the patient died. One patient was lost to follow-up. 10 patients survive more than five years.

**Discussion:** Incidence of brainstem glioma in children can be accounted for within a 10-20% of primary tumors. The tectal plate gliomas belongs to a rare type. The incidence of glioma in children is less than 5%. Slow growth, years of follow-up imaging results are stable. Most of the patients with glioma of mesencephalon tegmental region are seeing a doctor due to the hydrocephalus. The treatment of endoscopic third ventriculostomy for obstructive hydrocephalus caused by tectal plate gliomas is an effective means. After alleviating hydrocephalus, the patients can live for a long time. Regular follow-up with MRI is needed for the patients.

## P59

### Pre-and postoperative cerebral blood flow changes in patients with idiopathic normal pressure hydrocephalus measured by computed tomography (CT)-perfusion

Doerthe Ziegelitz<sup>1\*</sup>, Jonathan Arvidsson<sup>2</sup>, Per Hellström<sup>3</sup>, Mats Tullberg<sup>3</sup>, Carsten Wikkelsö<sup>3</sup>, Göran Starck<sup>2</sup>

<sup>1</sup>Neuroradiology, Clinical Sciences, Sahlgrenska Academy at University of Gothenburg, Sweden; <sup>2</sup>Radiation Physics, Clinical Sciences, Sahlgrenska Academy at University of Gothenburg, Sweden; <sup>3</sup>Clinical Neuroscience and Rehabilitation, Neuroscience and Physiology, Sahlgrenska Academy at University of Gothenburg, Sweden

E-mail: doerthe.ziegelitz@vgregion.se

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**Introduction:** Computed tomography perfusion (CTP) is an established technique, but has not yet been applied to idiopathic normal pressure hydrocephalus (iNPH), in which cerebral blood flow (CBF) is of pathophysiological, diagnostic and prognostic interest. The aim of this work was to determine the pre-and postoperative regional and global

CBF in iNPH by CTP, expecting the results to confirm the findings of a perfusion evaluation on the same group of patients and controls, previously performed with magnetic resonance perfusion (MRP).

**Methods:** CTP was performed in 18 iNPH patients pre- and 3 months postoperatively. One postoperative CTP was omitted from the analysis because of a confounding subdural hematoma. 6 healthy, age-matched individuals (HI) served as controls at baseline. The CTP covered 4 adjacent 5 mm sections immediately above the posterior commissure. CBF was calculated in 12 cortical and subcortical regions of interest. Besides group comparison of the CBF estimates and examination of individual, postoperative CBF changes, also the correlation of CBF and the severity of symptoms was analyzed. Probable iNPH was diagnosed based on the iNPH Guidelines and clinical performance was assessed according to a newly developed iNPH scale.

**Results:** The preoperative CBF in iNPH patients was significantly reduced in the normal appearing and periventricular white matter (PVWM), the lentiform nucleus and the global parenchyma. No CBF differences were found between responders and non-responders. After shunt diversion CBF increased in responders in all anatomical regions by 2.5-32 % to the perfusion level of HI, but remained significantly reduced in the PVWM of non-responders. The pre-and postoperative CBF of cortical and subcortical regions correlated with the intensity of symptoms and the total iNPH scale score.

**Conclusions:** In spite of limited spatial coverage, CTP can measure CBF changes in iNPH. CTP confirmed largely previous MRP-based results, indicating the reliability of both perfusion methods.

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## P60

### Assessment of ventriculo-peritoneal (VP) shunt malfunction in an in vitro model of artificial CSF flow: influence of CSF protein concentration, CSF contamination and time of shunt incubation

Thomas Joseph Zwimpfer<sup>1\*</sup>, Matthew Joseph Zwimpfer<sup>2</sup>

<sup>1</sup>Vancouver Gen. Hosp., U. of British Columbia, Canada; <sup>2</sup>School of

Engineering & Applied Science, U. of Pennsylvania, USA

E-mail: zwimpfer@mail.ubc.ca

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**Introduction:** Experiments were carried out in an In Vitro model of CSF flow through VP shunts (Medtronic Inc) to investigate the influence of three factors on shunt function: 1) CSF protein concentration; 2) CSF contamination and; 3) Time of shunt incubation in the artificial CSF.

**Methods:** Two components of a shunt were tested separately: 1) Ventricular catheter and; 2) Medium pressure, non-programmable valve connected to a peritoneal catheter. In the "sterile" artificial CSF groups, each shunt was incubated in one of six different sterile solutions of varying protein conc. (0.5 g/l - normal and 1.0, 2.0, 5.0, 10.0 and 20 g/L), prepared by adding egg protein ("Naturegg" Egg Whites; 1g/9ml) to normal saline, and incubated in sterile artificial CSF for periods of 0, 7, 14 and 46 days.

A "Contaminated" group of shunts were similarly prepared but exposed to skin microbes by handling them with ungloved hands and incubating them in contaminated artificial CSF. The same contaminated CSF solutions were used over the total 46 days of incubation but only 3 different protein conc. (0.5, 5.0 and 20.0 g/L) were prepared.

Both the sterile and contaminated shunts were tested after four different incubation periods (0, 7, 14, 46 days). Each of the two shunt components (1. Ventricular and; 2. Valve/peritoneal catheter) were tested separately by connecting them with I.V. tubing to a manometer, all filled with the test CSF. The manometer was prefilled to a height of 30 cm H2O and CSF was allowed to flow through each shunt component. The elapsed time (s) was recorded when the CSF passed each 5cm increment from 30 to 0 cm H2O or until flow stopped above 0 cm. On a few occasions, CSF did not drop from the 30 cm level. This "shunt blockage" occurred only when testing the valve

/ peritoneal catheter complex. Height of CSF column (cm) was plotted against time and the best linear fit determined for each data set. The slope of each curve approximated the average rate of CSF flow (cm/s).

**Results:** In this In Vitro model, CSF protein of 5g/L or higher was the threshold level to adversely affect CSF flow through the valve/peritoneal catheter component: Incubation for 46 days in a protein conc. of 10 g/L or higher, resulted in a 75% decrease in CSF flow rate (.07 cm/s) and an elevated closing pressure of 11 cm H<sub>2</sub>O, compared to testing at day 0 in 0.5 g/L (rate = .30 cm/s; CP = 6 cm H<sub>2</sub>O). Microbial contamination did further slow flow but only after 46 days incubation in CSF with a protein conc. of greater than 5 g/L. Absence of cellular and humoral mediators of inflammation in this artificial CSF could be addressed in future studies by

using CSF from patients with proven shunt infection. Flow through the ventricular catheter was not affected in any situation in this model.

**Cite abstracts in this supplement using the relevant abstract number, e.g.:** Zwimpfer and Zwimpfer: Assessment of ventriculo-peritoneal (VP) shunt malfunction in an in vitro model of artificial CSF flow: influence of CSF protein concentration, CSF contamination and time of shunt incubation. *Fluids and Barriers of the CNS* 2015, 12(Suppl 1):P60