Targeting autoregulation-guided cerebral perfusion pressure after traumatic brain injury (COGiTATE): a feasibility randomized controlled clinical trial

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Aim: Recent studies have suggested inflammation as a source of membrane formation and continued haemorrhage in Chronic Subdural Haematoma (CSDH). This study aimed to analyse CSDH content for a range of inflammatory markers to improve understanding of the mechanisms involved and assess response to dexamethasone.

Method: Participants recruited to the Dex CSDH trial undergoing surgery were eligible for inclusion. Peripheral blood and CSDH fluid were collected intra-operatively and post-operatively for up to 72 h. A magnetic bead-based immunoassay (Luminex) measured a panel of 12 inflammatory markers and was correlated with recurrence and dexamethasone use.

Results: Data from 51 patients over 56 operations were included. All but one of the inflammatory markers measured were significantly elevated in CSDH fluid compared to peripheral blood; Vascular Endothelial Growth Factor (VEGF) was consistently the highest. Three pro-inflammatory markers were significantly raised in recurrent compared to primary CSDH, and significantly lower levels of interleukin-10 (IL-10) were seen in CSDHs that went on to recur compared to those that didn’t (p = 0.0015). Most markers showed increased concentrations post-operatively, peaking at 48 h. Patients treated with dexamethasone showed a significant reduction in VEGF at 48 h post-operatively.

Conclusion: This data supports the theory of a localised inflammatory response in CSDH, with VEGF a critical factor. A reduced anti-inflammatory profile (IL-10) in primary CSDH may increase the risk of recurrence. A reduction in post-operative VEGF with dexamethasone exposure may be a mechanism by which dexamethasone reduces recurrence. Further research should be focused on therapies targeting VEGF.
Global neurotrauma outcomes study spine: an international, multi-centre, prospective observational study on traumatic spinal injury

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Aim: Traumatic spinal injury (TSI) accounts for a significant proportion of disability and death worldwide, with the majority of this burden affecting individuals in low- to middle- income countries. The current global approach to the care of patients following TSI is inconsistent with considerable geographical differences reported, and limited data available on the impact of these variations on outcomes following TSI. On this background, we aim to provide a comprehensive international picture of the case-mix, processes of care and variations in non-operative and operative management strategies, including emergency, ward, ICU care, in patients presenting with traumatic spinal injury (TSI).

Method: A multi-centre, international, prospective, observational study. Any unit assessing patients with TSI worldwide will be eligible to participate. All adults with radiologically confirmed TSI will be included, in any given consecutive 30-day period in a given participating unit within the 6-month study period. Each participating unit will form a study team responsible for gaining local approval, identifying patients for inclusion and conducting data collection. Processes of care will be characterised on registration through a detailed provider profiling exercise. Data will be collected via a secure online platform in an anonymised form.

Results: The dataset, developed through an iterative feedback process involving clinicians from low and high Human Development Index (HDI) countries, includes patient demographics, details of injury mechanism, local injury management and, if applicable, timing and nature of surgery, post-operative care and immediate post-operative complications. Outcome measures include Frankel grade at 6 weeks post-admission (or at discharge or death, whichever event occurs first), early mortality, peri-operative complications, adverse events of special interest, functional status and mobility. Descriptive analyses of case-mix and the variations in processes of care will be conducted. Available resources, use of guidelines and variations in processes of care will be characterised using both provider profiling responses and patient-level data collected. Areas where known best practice is deficient or unavailable will be identified as potential targets for future implementation studies.

Conclusion: GNOS Spine aims to provide a global snapshot of the case-mix, management and short-term outcomes of patients with TSI. In addition, we aim to identify areas for further study, and establish a platform and clinical network to facilitate future research in global spinal trauma and neurosurgery.

Utilising human induced neurons to emulate secondary injuries of traumatic brain injury – exploration of disodium succinate as a rescue agent

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Aim: We aimed to study metabolic dysfunction and inflammation in induced human neurons (iNs) as a model for traumatic brain injury (TBI), and subsequently to assess the efficacy of the potential neurotherapeutic agent, succinate, for ability to rescue metabolic function. Rotenone is an inhibitor of complex I of the mitochondrial transport chain and lipopolysaccharide (LPS) is a bacterial membrane protein that interacts with receptors, triggering an immune response and release of pro-inflammatory cytokines. By measuring levels of extracellular glucose, lactate and pyruvate, particularly the latter two, the cellular metabolic state can be deduced. It has been suggested that a high lactate/pyruvate ratio (LPR) indicates increased glycolysis and reduced mitochondrial activity, \textit{in-vivo}, and high brain extracellular LPR \textit{in-vivo} correlates with unfavourable patient outcome (1). This work

Method: We hypothesised that disodium succinate could rescue metabolic dysfunction and inflammation in iNs exposed to LPS and Rotenone. Human induced neurons (iNs) were generated from CD133+ neural stem cells by using a human induced pluripotent stem cell approach, and cultured to maturity (~20 days) in a medium supplemented with nerve growth factor and BDNF. Non-induced neural stem cells were used as controls.

Results: It was observed that iNs responded to Rotenone by increased lactate production and decreased glucose consumption. This was blocked by concurrent treatment with disodium succinate. In the presence of LPS, cell viability was reduced, and this was significantly increased when succinate was administered concurrently.

Conclusion: These findings suggest that iNs are a useful model for the study of secondary injuries following TBI and that disodium succinate has potential as a rescue agent in this setting.
Resveratrol attenuates endoplasmic reticulum stress (ERS) induced cell death and results in functional improvement after traumatic brain injury

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\textbf{Aim:} Resveratrol (RSV), a polyphenol antioxidant, has been reported to function as a neuroprotector. We explored the molecular mechanisms that underlines the anti-inflammatory activity of RSV in traumatic brain injury (TBI) in mice relevant to endoplasmic reticulum stress (ERS). By establishing three experimental groups (sham, TBI, and TBI + RSV), we examined the effects of RSV after TBI on ERS and caspase-12 apoptotic pathways cascades. The protein expressions levels of C/EBP homologous protein (CHOP), glucose regulated protein 78kD (GRP78), caspase-3, and caspase-12 in cortical brain tissues were evaluated by western blotting. The cortical brain tissues were also subjected to a qPCR analysis of mRNA expression of tumor necrosis factor (TNF)-\textalpha and interleukin (IL)-1\textbeta. Additionally, immunofluorescence staining was used to determine the expression of GRP78 in microglia and neurons. The neurological function of the mice was analyzed based on modified neurological severity scores (mNSS).

\textbf{Method:} 54 mice were randomized into three groups: a sham operation group (n = 18), a TBI group (n = 18), and a TBI group treated with RSV (TBI + RSV, n = 18). All experiments were performed in a blinded manner. TBI + RSV mice were treated with an intraperitoneal RSV injection (40 mg/kg) immediately after establishment of the TBI model and then daily up to 3 d after TBI. The protein expressions levels of C/EBP homologous protein (CHOP), glucose regulated protein 78kD (GRP78), caspase-3, and caspase-12 in cortical brain tissues were evaluated by western blotting. The cortical brain tissues were also subjected to a qPCR analysis of mRNA expression of tumor necrosis factor (TNF)-\textalpha and interleukin (IL)-1\textbeta. Additionally, immunofluorescence staining was used to determine the expression of GRP78 in microglia and neurons. The neurological function of the mice was analyzed based on modified neurological severity scores (mNSS).

\textbf{Results:} After RSV treatment, the expression of CHOP, GRP78, caspase-3 and caspase-12 decreased, and qPCR results showed downregulation of TNF-\textalpha and IL-1\textbeta. Immunofluorescence stain demonstrated Iba-1\textsuperscript{+}/GRP78\textsuperscript{+} and NeuN\textsuperscript{+}/GRP78\textsuperscript{+} cells decreased after RSV treatment. The mNSS analysis indicated improvement following RSV treatment.

\textbf{Conclusion:} In conclusion, we found that RSV treatment can relieve secondary brain injury and protect brain tissue after TBI by affecting ERS, apoptosis, and neuroinflammation. This study shows that RSV may become an important treatment for TBI disability.

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Quantifying and drawing associations of pro and anti-inflammatory cytokines in human cortical inflammation after traumatic brain injury

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Aim: Traumatic brain injury (TBI) is one of the leading causes of morbidity and death globally. Animal models and patients CSF studies have demonstrated a strong inflammatory response to TBI. However, anti-inflammatory drugs tested in animal models have failed to improve clinical outcomes in multiple clinical trials. This highlights the urgent need for a model of human-TBI that can be utilised for preclinical anti-inflammatory drug screening before taking it onto more time-demanding and expensive clinical trials.

Method: We herein describe and validate the use of a weight drop model of human 3D cell cultures to examine post-traumatic injury neuroinflammation and cell death. Cell death in cultures is quantified using the cell death marker propidium iodide (PI) and live cell imaging. Neuroinflammation is tested on the basis of the release of the damage-associated molecular pattern protein: HMGB1. Furthermore, we quantified the concentrations of a panel of pro-inflammatory and anti-inflammatory cytokines using Meso-Scale Discovery (MSD) V-PLEX technology at 24 and 72 h post-injury.

Results: We show in an ex vivo model of human brain tissue that drop-weight injury results in extensive cell death and a significant release of the master-switch of neuroinflammation HMGB1 at 24 h. Subsequently, there was a slight decrease in the concentrations of pro-inflammatory cytokines at 24 h post-injury, but this was not statistically significant until the 72 h time point. Similarly, we observed an initial drop of the anti-inflammatory cytokines at 24 h followed by a significant effect by 72 h post-injury.

Conclusion: Our results show that HMGB1 is released well before other inflammatory cytokines; the causal-effect relationship is to be confirmed. The increase in both pro-and anti-inflammatory cytokines at 72 h post-injury highlight the double-edged nature of post-traumatic injury in human; this will need to be taken in consideration from drug-discovery perspective.

Can manipulation of neuroinflammation modulate oligodendrogenesis and white matter repair after TBI?

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Aim: Whilst traumatic axonal injury (TAI) is a key hallmark of traumatic brain injury (TBI), there is an unmet clinical need to develop greater mechanistic understanding of white matter injury after TBI. High-mobility group box 1 (HMGB1) is implicated as a regulator of brain inflammation, and its elevated levels in the CSF after TBI is associated with worse outcomes. The aim of this project is to investigate the effect of HMGB1 upon oligodendrocyte progenitor cells (OPCs) in an in vitro model of TBI in rodents and then validate those findings in a human model.

Method: We examined the temporal release of HMGB1 post-trauma in a reductionist model of needle scratch injury in 2D rat cortical cell cultures then validated this in a weight-drop model of TBI in 3D adult human cortical cell cultures. ELSA, immunohistochemistry and western blot used to profile HMGB1 release and subsequent roles in neuroinflammation. We utilised immunohistochemistry to quantify the effect of injury condition medium (ICM) on oligodendrocyte progenitor cells proliferation, survival and differentiation in the rate cultures.

Results: We demonstrate the release of HMGB1 in rat 2D and human 3D cell cultures. In both models we further demonstrate that HMGB1 resulted in robust proinflammatory response. Intestinally, while microglia were the source of HMGB1 in rat cultures subjected to trauma, preliminary data demonstrate that NG2 cells also contribute to HMGB1 release in the human model. In the rat model ICM resulted in a significant decrease in the numbers of NG2+ cells compared to standard control conditions. Co-treatment with BoxA (HMGB1 blocker) completely abolished ICM-induced NG2+ cell loss.

Conclusion: Our animal data clearly demonstrate a detrimental effect of post-TBI HMGB1 on oligodendrogenesis. Whilst our data in the human 3D cultures are preliminary, they clearly recapitulate observation of HMGB1 release in other animal TBI models.

The CONTACTS study; investigating the diagnostic utility of salivary micro-RNA in identifying concussion in NHS patients. On ongoing study

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Aim: The diagnostic utility of salivary micro-RNA (mRNA) in the identification of sports-related concussion made headlines earlier this year. Research conducted with English Rugby Union players demonstrated a unique panel of 14 salivary mRNAs expressed in players with clinically confirmed concussion compared with controls. The translatability of this test to NHS patients must be explored given the complexity of concussion diagnosis outside of professional sport. The aim of the CONTACTS study is to determine whether salivary mRNA can differentiate concussed from control participants in a non-athlete sample. An additional aim is to assess the utility and translatability of commonly used sports-concussion assessment tools in NHS patients; the Sports Concussion Assessment Tool version 5 (SCAT5) and the Immediate Post-concussion Assessment and Cognitive Testing (ImpACT).

Method: The CONTACTS study is a two-phase prospective cohort study sponsored by the University of Birmingham. For the initial feasibility phase, we aim to recruit 30 participants; 15 with maxillofacial trauma and a clinical diagnosis of concussion and 15 with isolated orthopaedic limb trauma. Saliva samples will be taken in the Emergency Department (ED) and at 24–48 h. Samples will undergo next generation
 sequencing to identify mRNAs. ImPACT and SCAT5 assessments will be undertaken at the same timepoints and remotely at 14 days. Ethical approval has been gained and recruitment is underway at the Queen Elizabeth Hospital Birmingham.

Results: Data analysis for the feasibility phase will be descriptive and mainly focus on confidence interval estimation, with no hypothesis testing performed. Analysis of the initial phase data will determine the recruitment target for phase two.

Conclusion: Currently the diagnosis of concussion in patients presenting to the ED is difficult, with only 23% actually being diagnosed. An objective diagnostic test would be a game-changer in the identification of patients suffering concussion. Improving diagnosis has wide-reaching implications beyond improving the acute clinical management of our patients. A more accurate epidemiology of concussion would be possible aiding any funding decisions for services or future research. Traditionally patients with cognitive impairment, psychiatric disease or concurrent intoxication have been excluded from concussion studies due to diagnostic difficulties. Being able to definitively identify concussion in such groups would increase the likelihood of these patients being included in research. The NICE Head Injury guidelines highlight the need for research into diagnostic head injury biomarkers and salivary mRNA has proven a worthy candidate for investigation. The CONTACTS study aims to take existing research in sports to the wider NHS population.

Mid-infrared spectroscopy for cerebral microdialysate metabolite monitoring

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Aim: The brains of patients suffering from traumatic brain injury (TBI) undergo dynamic biochemical changes in the days following the initial trauma (1). Timely monitoring of these changes is of paramount importance for early warning of adverse variations, allowing prompt treatment and maximising the opportunity for improving patient outcome. Our aim is to develop a sensor system based on mid-infrared (mid-IR) spectroscopy, which would allow automated and continuous online monitoring of glucose, lactate, and pyruvate, three clinically relevant substances in TBI-patient microdialysate, over several days at the patient bedside. Based on existing evidence, such a system would be of great value and highly beneficial for clinicians, nurses, and most importantly for favourable TBI-patient outcome.

Method: Mid-IR spectroscopy allows rapid, reagent-free, molecular fingerprinting of liquid samples, and can be easily integrated with microfluidics. We used mid-IR transmission spectroscopy to analyse glucose, lactate, and pyruvate, three relevant brain metabolites, in the extracellular brain fluid of two TBI patients, sampled via microdialysis (2). Microdialyses were collected hourly, then pooled (3 – 4 h), and measured consecutively using the standard ISCUSflex analyser and the mid-IR sensor system. The mid-infrared sensor comprises a quantum cascade laser (QCL), a detector and a transmission flow-cell of specified path-length, through which the microdialysis sample flows. Upon light-sample interaction within the flow-cell, the portion of light which is not absorbed by the sample reaches the detector, resulting in absorbance spectra. We employed partial-least-squares regression (PLSR) to compute concentrations from absorbance spectra. The resulting concentrations were then compared to those obtained using the conventional ISCUSflex microdialysis analyser.

Results: Detection limits of 0.5, 0.2, and 0.1 mM were achieved for pure glucose, lactate, and pyruvate, respectively, in perfusion fluid using the mid-IR sensor system with an integrated transmission flow-cell. A strong correlation was observed between the compound concentrations obtained using the conventional ISCUSflex analyzer and the mid-IR sensor. This study demonstrates the potential utility of mid-IR spectroscopy for continuous, automated, reagent-free, and online monitoring of the dynamic chemical changes in TBI patients, allowing a more timely response to adverse brain metabolism and consequently improving patient outcomes.

Conclusion: The performance of mid-IR spectroscopy was evaluated as a technique to analyse and monitor the brain chemistry of TBI patients. While our system allows coverage of most of the physiological range for glucose and lactate, it proved challenging to detect pyruvate, because it is present at much lower concentrations in the brain. A high correlation was seen between patient microdialysate concentrations obtained using the mid-IR sensor and the ISCUSflex analyser, for glucose and lactate. The developed PLSR model showed promising results in predicting the concentrations of the relevant compounds in patient microdialysate samples. This study demonstrates the feasibility of using mid-IR spectroscopy for monitoring the dynamic changes in TBI patients’ brain chemistry over several hours and days. Further work will focus on improving the sensor sensitivity as well as demonstrating continuous online microdialysis monitoring in TBI patients.

Continuous neurochemical measurements in traumatically injured brain using a microdialysis coupled mid-infrared sensor

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Aim: Abnormal glucose concentrations (low and high) and elevated lactate/pyruvate ratio (LPR >25) that indicate brain metabolic disturbances have been reported in brain microdialysates of severe TBI patients resulting in unfavourable clinical outcomes. Cerebral microdialysis (CMD) conventionally allows hourly measurements using a bedside analyser. However, metabolic changes in an injured brain can be more rapid and it is imperative that dynamic changes are continuously monitored, thereby enabling timely clinical interventions to treat adverse brain metabolism, consequently improving patients’ outcomes. Here, our aim was to
Improving risk prediction for aneurysmal subarachnoid haemorrhage (aSAH) patients

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Aim: Well calibrated models with good discrimination have been published for aneurysmal SAH. These models are devised on the assumption that the overall effect equals the sum of the attributes and do not account for the fact that variables are often inter-related.

Method: Data on 10376 aSAH patients from the UK and Ireland SAH database were analysed using a logistic regression model of the dependence of outcome at discharge on predictors measured during in-hospital treatment at a neurosurgical centre. The complexity of the model was gradually increased by sequentially incorporating non-linear spline relationships for “age” and “calendar time,” and “age” * “treatment,” “grade” * “EVD” interaction terms. Goodness of fit was assessed using pseudo $R^2$ and Akaike information criterion. We compared accuracies of models’ predictions based on the value of the Brier score.

Results: There were significant nonlinearities in the effects of “age” and “calendar time.” “Age” * “treatment” and “grade” * “EVD” interactions were also highly significant, and their introduction in the model improved all the goodness-of-fit criteria employed.

Conclusion: Increasing the complexity of the aSAH model may improve prediction accuracy. Potential causal interpretations of the results will be discussed.
Results: In this presentation we present the interim results from analysis of the first 70 aneurysms with 215 post contrast scans. In paired images post contrast delay beyond 2 min did not significantly affect measurements. Nor did voxel size, but clear differences in intensity were seen as anticipated with changes in head coil, and slab thickness (i.e. signal-to-noise). In unpaired images from different scanners large changes in intensity were noted as also may be anticipated. After normalisation of values, there were no statistically significant differences in the amount of variability between different non enhancing structures or between different enhancing structures, to clearly justify selection of one over another, although some trends were noted that may become significant with greater numbers of scans analysed that can be taken forwards for testing of indices for prediction of unstable aneurysms.

Conclusion: VWI shows great promise as a tool to predict risk of UIA instability and select cases for treatment. However, there can be significant differences in images depending on scanner and protocol used. These can be corrected through appropriate indexing against other structures in the image. This work to standardise measurements is an essential step that opens up the possibility of prospective multicentre trials of VWI to predict UIA rupture.

**ONCOLOGY SESSION**

**Real-time, passive visualisation of glioblastoma during surgery**

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**Aim:** The aim of this study was to investigate the feasibility of intra-operative visualisation of glioblastoma using long-wavelength passive infrared (i.e. thermal) imaging integrated with advanced digital image processing. Cancer cells reprogram their metabolism to enable generation of biomass and overcome bioenergetic and redox stress. The integrated elevated metabolic rate results in a raised thermal emissivity according to the Stefan and Boltzmann equation. Previous research studies reported a temperature difference between the normal tissue and the tumour of up to 3.3 °C. The literature suggests such thermal profile of brain tumours can be visualised using thermal imaging as a non-invasive approach. However, the accuracy of tumour margin delineation was not clinically acceptable due to technical limitations. We hypothesised that integrating high-resolution thermal camera with innovative image processing algorithm could optimise the signal-to-noise ratio and ultimately, offer an accurate intraoperative neuroimaging technology to improve surgery outcomes.

**Method:** Consented patients at the Cambridge University Hospital participated in this study just during their routine care. We used a hand-held custom-built imaging device to acquire images during the resection while care was taken to ensure that no peripheral heat sources were reflected into the field of view. The camera had resolution of 640 × 480 pixels/30Hz and thermal sensitivity of ~4mK at 30 °C in the spectral range of 7.5–13μm. It converted the infrared into an electrical signal and generated a monochrome image. We also acquired a copy of microscopic images from 5-ALA (i.e. NHS gold standard) to confirm the feasibility of our technology. The captured images were initially corrected for non-linearity/uniformity. Subsequently, we enhanced the immune clonal threshold segmentation technique by integrating temporal and spectral features embedded in grey levels of pixels. We partitioned thermal images into tumour and background by addressing the challenge of the fuzzy of edge (i.e. tumour margin).

**Results:** Thermal images were captured using our customised hand-held device. We assured that the fluorescence spectrum of 5-ALA is out of the working wavelength of our camera. Our proposed segmentation technique was compared with traditional fixed, adaptive and immune clonal thresholds. The maximum Euclidean distance between two segments (i.e. tumour and non-tumour) was achieved using our technique. Also, we compared the performance of our algorithm by comparing true positive and false positive rates with the gold standard 5-ALA which demonstrated thermal imaging can be successfully applied to gliomas visualisation.

We noticed depth of penetration (several microns) is not a limitation in practice because as the operation takes place, it is possible map inside the resection cavity to sample the deeper tissue. This implies that thermal imaging with advanced image processing holds a great promise as a non-invasive intraoperative neuroimaging platform.

**Conclusion:** We demonstrated the feasibility of brain tumour visualisation using thermal imaging to optimise neurosurgical planning. The growing enhanced immune field proposed herein has a good growth factor for blurry edges of the infrared image target. Hence, our proposed thermal imaging with integrated advanced software addressed the challenge of poor accuracy of previous research studies. It is proposed to run a more extensive clinical validation study where our technology will be validated against biopsy to demonstrate non-inferiority and/or superiority of our technology with respect to 5-ALA. This should be followed by the development of an AI platform for automatic segmentation of brain tumours delineation. Furthermore, human factor studies should be considered to further investigate the best adaptation strategy.

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**Surgical resection for glioblastoma is associated with white matter changes connecting hub-regions**

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**Aim:** Surgical resection is the primary treatment for glioblastoma. However, it is associated with risk of injury to the brain. The breakdown of the blood-brain barrier plays a central role in the process of surgical injury, leading to oedema and tissue damage. (1) White-matter tracts are especially vulnerable. Gliomas preferentially invade white-matter and may be found in regions of high connectivity, known as hub-regions of the brain. (2) Diffusion MRI is sensitive to the movement of water molecules and may be able to identify structural changes associated with surgery. We hypothesise that changes in extracellular water measured with diffusion MRI are associated with surgery and that these changes are in white-matter connecting hub-regions of the brain.

**Method:** 12 patients with glioblastoma underwent preoperative and postoperative imaging with structural and diffusion MRI within one-week before surgery and within 72h post-surgery at a single centre. Single-tensor and two-tensor free water elimination models were fitted to the pre-processed diffusion images. These models generated voxel-wise maps of Fractional Anisotropy (FA), FA, free-water corrected, and Free-water. Tract-based Spatial Statistical analysis (TBSS) was performed using a paired t-test to compare preoperative and postoperative images. Permutation-based, non-parametric
Understanding the risks to cognitive function and the early timeframe of recovery after surgery for glioblastoma: tools to help patient and carer counselling

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**Aim:** Despite extremely high rates of cognitive deficits in patients undergoing glioblastoma surgery (1), the data and means used to convey these risks to patients and carers could be improved. We aim to present data regarding these risks longitudinally from before to after glioblastoma surgery and show the scope for recovery of deficits between the early postoperative phase to the period before radiotherapy. We will present this data in conventional odds risk formats as well as on risk spectra and frequency pictographs/waffle plots commonly used in primary care.

**Method:** A prospective study (CogENT) using electronic cognitive testing delivered by the OCS-Bridge tablet computer based tool (2), assessed participants undergoing glioblastoma surgery before operation (T0), early post-operatively (<2 weeks; T2) and late postoperatively but before radiotherapy (4–6 weeks; T3). The results were compared to normative data from a sample of healthy volunteers on the same electronic tests. Test results consistent with deficit were defined as 2SD from healthy normative scores, in keeping with the lowest 5–10% of those performances. All risk calculations and data visualisations were performed using the “epitools” and “exact2by2” packages in R.

**Results:** 49 participants were recruited. The overall risk of any cognitive deficit before surgery was 96% (47/49) and early after surgery was 100% (49/49). The domains in order of highest risk were attention (pre-operative OR = 39, post-operative OR = 1401, p = 0.0002), perception (pre-operative OR = 214, post-operative OR = 260, no significant difference), memory (pre-operative OR = 97, post-operative OR = 185, no significant difference), language (pre-operative OR = 6, post-operative OR = 19, p = 0.01), praxis (pre-operative OR = 3, post-operative OR = 12, p = 0.01) and number (pre-operative OR = 4, post-operative OR = 7, no significant difference). A multi-variate analysis was performed including clinical, radiological and treatment factors. Only age and IDH mutant status had an interaction with cognitive performance in the perception domain. Cognitive function improved from T2 to T3, with odds of cognitive deficit returning to similar levels as T1 or slightly better. For attention, perception and memory these risks remained significantly higher than healthy control performance.

**Conclusion:** OCS-Bridge addressed an area of unmet need for these patients who otherwise would not have undergone longitudinal cognitive testing by conventional pen-and-paper assessments delivered by neuropsychologists. This data and its visualisations can help patients and carers understand the risks from glioblastoma surgery and the potential for recovery after 4–6 weeks, especially as the public is more familiar with data visualisations during Covid-19 news reporting. It also provides the basis for a window in which to focus rehabilitation interventions to maximise a recovery process that is demonstrated in the data.

Microglia drive interferon-dependent zika virus resistance in GBM

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**Aim:** Cancer stem cells are thought to drive tumour growth and therapeutic resistance by co-option of fundamental developmental mechanisms. However, efficient targeting of glioma stem cells in glioblastoma multiforme (GBM) remains an elusive goal. Zika virus (ZKV), a flavivirus, shows tropism for SOX2+ stem cell populations in both the early human developing brain (HDB) and GBM. We set out to investigate the potential of Zika Virus as an oncolytic, and to derive insights into glioma stem cell targeting.

**Method:** Primary patient GBM and human developing brain (HDB) tissues harvested at operation and termination respectively were analysed in slice culture format, or dissociated to single cell suspensions for adherent culture with or without antibody-based magnetic sorting of specific cell fractions. Samples were infected with wildtype PE243 South American strain Zika Virus and/or a transgenic mCherry reporter expressing strain, and processed for virus levels by qRT-PCR, marker expression by IF and RNA-Scope, and expression profile using bulk and single cell RNA-sequencing.
**Results:** We report that patient-derived primary GBM samples are highly resistant to ZKV infection compared to human developing brain, despite shared stem cell identities. We found that GBM resistance correlates with an innate immune expression signature and reveal that isolated patient GBM microglia/macrophages (MG) were necessary and sufficient to confer glioma stem cell resistance to ZKV infection. The tumour microenvironment MG secreted antiviral cytokines in response to viral challenge or mimetics. Remarkably, the interferon-β (IFNβ) pathway JAK1/2 inhibitor, ruxolitinib, reversed the effect of patient-derived MG conditioned medium and restored Zika infection and oncolyis.

**Conclusion:** Our findings indicate that the microglial secretome establishes an antiviral transcriptional state and resistance in glioma stem cells, and that JAK inhibitors enhance human GBM susceptibility to oncolytic ZKV infection.

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**A pilot study of utilising volumetric analysis to guide management of meningioma – has it changed in size and does it matter?**

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**Aim:** Meningiomas are frequently detected as incidental findings in neuroimaging performed for non-specific neurological symptoms. It is conventional wisdom that meningiomas grow slowly. Accordingly, many incidental meningiomas are managed conservatively with serial cranial imaging. Treatment decisions by the multi-disciplinary team (MDT) are deferred until there is evidence of growth on radiological reporting. We have evaluated the use of commercially available segmentation volumetric analysis (SVA) software to analyse the growth pattern of a cohort of incidental meningiomas.

**Method:** A service evaluation project of the Siemens Syngo.via volumetric analysis software package. The MRI scans (gadolinium-enhanced T1-weighted sequence with slice thickness of ≤3 mm) of 20 consecutive patients with peripherally positioned incidental meningiomas diagnosed between 1/1/2013 and 31/12/14 were analysed. Two authors (JXL, Year 2 AFP doctor and RB, senior reporting radiographer) independently performed segmentation volumetric measurements. Three automated and manual segmentation volumetric measurements were performed for each MRI study to calculate the mean tumour volume. The presence of growth based on SVA (defined as >10% volume increase over 12 months) was compared with radiologists’ reports for agreement. The inter-rater reliability was assessed using Intraclass correlation coefficients (ICC). Bland-Altman plot was done to look for agreement between SVA measurements performed by the analysts. The tumour volumes obtained from automated and manual SVA were also compared for discrepancy using T-tests and ICC.

**Results:**
- 99 MRI studies from 20 patients (19F:1M, mean age:63) with incidental meningiomas (17 convexity and 3 anterior cranial fossa tumours) were analysed.
- Median follow up was 46 months (Interquartile range: 27.25–84.5) and an average of 5 scans per patient (Range: 2–10). Based on a 95% confidence interval, the calculated ICC was 0.992 indicating highly significant inter-rater reliability. Bland-Altman plot showed that there was a consistent level of agreement between the independent volumetric measurements performed by JXL and RB across the range of tumour volumes.
- Automated measurements were consistently larger than manual measurements (Range: 2–13%) but they have a linear relationship with an ICC of 0.999 highlighting high level of consistency. The SVA results concordance with radiologist report for presence in growth was 63% (50 of 79).
- Automated volumetric acquisitions take 1–2 min to perform per study with additional 7–8 min to do manual perimeter adjustments.

**Conclusion:** Previous studies have shown that majority of meningiomas grow in size over time and often the growth pattern is complex. Serial monitoring and clinical review are crucial in the conservative management of cases of incidental meningioma. In this pilot study, we have shown that segmentation volumetric analysis using commercially available software is accurate in detecting changes in tumour volume and straightforward to use. The objective evidence provided to the MDT can facilitate management decisions and more importantly allow informed discussion with patients. Further studies are required to validate these initial results and extend the scope of use to meningiomas in other intracranial locations.

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**Fibulin-2: a novel biomarker for differentiating grade II from grade I meningiomas**

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**Aim:** To assess Fibulin-2 as a molecular marker for differentiating between grade II and grade I meningiomas, by evaluating its expression in meningioma cells, tissue and blood plasma levels.

**Method:** 178 meningioma (87 grade I and 91 grade II) samples were used in this study. The tumours were reviewed and classified according to the 2016 edition of the Classification of the Tumours of the CNS. Fibulin-2 levels were assessed in meningioma primary cells via proteomic analyses, Western blotting and quantitative polymerase chain reaction (qPCR); in tissue via immunohistochemistry and qPCR; and in plasma via enzyme-linked immunosorbent assay (ELISA).

**Results:** Proteomic analyses (p < 0.05), western blotting (p < 0.05) and qPCR (p < 0.01) confirmed significantly higher Fibulin-2 expression levels in grade II meningiomas compared to grade I. To distinguish between grade I and II meningiomas, Receiver Operating Characteristic (ROC) analysis of Fibulin-2 RT-qPCR expression levels in meningioma tissue indicated an AUC of 0.73 (92% specificity and 26% sensitivity). Fibulin-2 blood plasma levels were also significantly lower in grade II compared to grade I meningiomas.
A prospective study of surgical management of symptomatic pineal cysts without hydrocephalus – an update from the first 21 cases

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Aim: There is currently no consensus on the safety and efficacy of surgical management of non-hydrocephalic symptomatic pineal cysts (nhSPC). The currently available evidence comes from retrospective case series and case reports and is, as such, associated with inherent shortcomings. Here, we present the protocol and provide an update from a prospective study on the surgical management of nhSPC. The aim of the study is to assess safety and efficacy of surgical management of nhSPC in an observational prospective cohort study. The aim of the presentation is to seek feedback of the Group on the design and conduct of the study.

Method: A prospective observational study to assess safety and efficacy of the surgical management of nhSPC (N=40, single centre, open to expansion). Every patient who underwent nhSPC surgery in Addenbrooke’s Hospital from April 2016 was administered two questionnaires to assess: (1) symptoms (bespoke, based on patient-reported symptoms in the literature and local clinical experience) and (2) quality of life (EORTC QLQ-C30) at the following time points: pre-operatively, 3 months, 12 months, 24 and 36 months post-operatively. All operations were performed by a senior consultant neurosurgeon (TS) at Addenbrooke’s Hospital, via supra-cerebellar infratentorial (SCIT) approach. Data were collected and anonymised in accordance with ethical and legislative standards.

Results: From April 2016 to September 2021 a total of 21 consecutive patients have received surgery for nhSPC in Addenbrooke’s Hospital, all of which were included in the study. Females composed 80% (17/21) of the cohort. Mean age was 36.4 years (range: 21–55). Mean follow-up was 214 days (range: 0–1095). Common presenting symptoms included headaches, visual disturbances, nausea and vomiting, dizziness and vertigo, sleep disturbance, gait abnormality, and fatigue. By the last follow-up, all patients reported experienced improvement of most of their symptoms and overall quality of life. There were no serious complications; two patients experienced impairment of eye movements.

Conclusion: The study is currently ongoing, but preliminary results are broadly in line with previously published retrospective data. Owing to the rarity of the condition we would welcome UK-based collaborations.

Automated Koos classification of vestibular schwannoma

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Aim: The Koos grading scale is a frequently used classification system for vestibular schwannoma (VS) that accounts for extrameatal tumor dimension and compression of the brain stem. The authors propose a novel artificial intelligence (AI) pipeline to fully automate the classification of VS from MRI to improve clinical workflow and facilitate patient management.

Method: The artificial neural networks were trained on a partly publicly available dataset of contrast-enhanced T1-weighted (ceT1) and high-resolution T2-weighted (hrT2) MR images from subjects with a single sporadic VS who were treated with Gamma Knife stereotactic radiosurgery on the day of the image acquisition. The first stage of the pipeline consists of a convolutional neural network (CNN) that segments the VS and 7 adjacent brain structures. For the second stage of the pipeline, we propose two complementary approaches that can be combined in an ensemble to enhance classification accuracy. One approach applies a second CNN, while the other approach is based on a random forest. Manual ground truth segmentations of the VS were determined in consensus by the treating team, consisting of a consultant neurosurgeon and physicist. Ground truth Koos grades were determined in consensus by a second team of experts including a consultant neuroradiologist and a consultant neurosurgeon.

Results: The automatic pipeline was assessed by comparing its classification accuracy, macro F1-score and weighted F1-score to that of two senior neurosurgical residents. Eligible patients (n=308) were randomly split into 5 groups to evaluate the model performance with 5-fold cross-validation. The weighted F1-score, macro F1-score, and accuracy of the ensemble model was assessed on the testing sets as follows: 89.3 ± 3.0/88.3 ± 4.2/89.3 ± 2.9, which is comparable to the performance of an average expert human annotator: 89.1 ± 5.2/88.3 ± 6.7/88.6 ± 5.8. Inter-and intraobserver reliability of the human annotators was comparable to results found in the literature. Interobserver reliability was assessed by calculating Fleiss’ generalized kappa (k=0.68) based on all 308 cases, and intrarater reliabilities of human annotator 1 (k=0.95) and human annotator 2 (k=0.82) were calculated according to the weighted kappa metric with quadratic (Fleiss-Cohen) weights based on 15 randomly selected cases.

Conclusion: The authors developed the first AI framework to automatically classify VSs according to the Koos scale. The excellent results show that the accuracy of the framework is comparable to that of expert human annotators and may therefore facilitate management of patients with VS. Moreover, the framework has the potential to be applied to other types of brain tumors.

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PHAB 1 – a pharmacokinetically guided, dose escalation study to assess the concentration of perphenazine in patients with high-grade primary brain tumours: a phase 1 clinical trial protocol

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Aim: Perphenazine is a derivative of the phenothiazine class of medications; a group of nitrogen and sulphur containing heterocyclic compounds labelled as first-generation typical antipsychotics.1 Perphenazine readily crosses the blood-brain barrier and has also been used to exert an antiemetic activity by blocking the dopamine and histamine-1 receptors. More recently, through application of a pharmacology gene expression signature platform, neurosurgeons and scientists have discovered potential anti-cancer properties of Perphenazine through exhaustion of the cancer cell bioenergetic energy.2 The primary aim of the PHAB-1 trial is to determine the exposure of high-grade brain tumours to pre-operatively administered Perphenazine within prospectively identified high-grade primary brain tumour patients through molecular examination of surgically resected tissues. Secondary aims included assessment of the safety profile (the Serious Adverse Event profile and Dose Limiting Toxicity) of Perphenazine.

Method: The PHAB-1 study is designed as an open-label, non-randomised, single-centre phase 1 clinical trial of Perphenazine given orally to patients prior to planned resection of a suspected primary high-grade brain tumour (diagnosed radiologically). Eligible participants will be enrolled in three-patient cohorts treated with Perphenazine administered three days prior to surgical resection, while being monitored for safety and dose limiting toxicity (DLT). In the first cohort, the dose administered will be 2 mg three times daily. Three patients will be enrolled to a cohort to assess each dose level. Dose escalation to a cohort of three new patients will occur when all patients in the previous cohort have completed the first full treatment regimen and no DLT has occurred. The pharmacokinetics of Perphenazine in the surgically resected tissue will be measured by hybrid liquid chromatography tandem mass spectrometry assay (LC-MS/MS).

Results: The primary endpoint is the presence of Perphenazine, or Perphenazine derivates in tumour (and other tissue) samples taken from surgical excision. Secondary endpoints include adverse events and laboratory toxicities. The clinical safety of Perphenazine will be monitored by reviewing the type, frequency and severity of any adverse events, regular haematological and biochemical laboratory tests, vital observations, and physical examination. This study is descriptive in nature and, at this phase, is not designed to provide analytical data regarding the anti-tumour efficacy of Perphenazine. Descriptive statistics will be used to summarise patient characteristics, methods used to administer the trial drug, and safety variables. All patients receiving a single dose of Perphenazine will be included in the safety analysis of the study.

Conclusion: Primary high-grade brain tumours are diffusely infiltrative, and a complete surgical resection is not possible. Since tumour cells are intermingled with healthy and potentially functional brain tissue, selective targeting at an effective dose is fundamental to success. To ultimately achieve this with any agent, it is important to identify the pharmacokinetics of Perphenazine in bulk tumour tissue first. Studies conducted on glioma cells have shown an apoptotic effect on the tumour cells without causing significant injury to non-cancerous cells. These studies, alongside evidence for blood-brain barrier penetration, make Perphenazine a potentially promising candidate to be used as a systemically delivered agent for managing high-grade primary brain tumours. The lack of in vivo studies relating to the use of Perphenazine against high-grade brain tumours further enhances the opportunity for practice-changing results to arise from this study.

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MISCELLANEOUS SESSION

Characterising short association fibre connections of the human cortex
C. Telco, D. Shastina and W. Gray

Aim: Short association fibres (SAF) are likely to represent as much as 60% of the total white matter of the human cortex. Despite this, SAF are relatively unstudied, due to their complex morphology and the limitations of diffusion MRI (dMRI) technology. A study of SAF connectomics has not been attempted on a large cohort, whole-brain scale. Using a combination of well-established tractography and connectivity analysis tools alongside a new SAF filtration method, this study aimed to create weighted SAF connectomes for a cohort of healthy young-adult subjects from the Human Connectome Project. This study also aimed to investigate the impact of streamline length chosen during the tractogram filtration process on resulting graph theory metrics.

Method: Weighted tractograms for each individual (64 subjects, Human Connectome Project Young-Adult S1200 cohort) were generated using SIFT2, which provides an estimate for the underlying axonal cross sectional area based on diffusion signal strength. By parcellating the connectome according to the Human Connectome Project’s Multi-modal Parcellation (Glasser et al., 2016), the cortical networks were compared using graph theory on both the individual and group-average scale. Graph theory, based on representing the brain as a network of brain regions (nodes)
connected by pathways (edges), removes the anatomical variation associated with individual brains and instead allows clear identification of regions of importance and connectivity patterns within the brain. Differences in graph theory metrics between streamline length groups were assessed by general linear modelling in R.

**Results:** By comparing the resulting graph theory metrics across three streamline length groups, this study demonstrates a significant difference in the connectivity of each streamline length group, and therefore highlights the importance of careful choice of streamline length and awareness of the effects this can have. We identified a collection of areas with larger connection strength and increased integration within the cortical network which tended to localise to the parietal lobe and primary somatosensory and motor regions, among other area of the brain associated mainly with sensory processing and cognition. We observed that areas with higher local connectivity and integration tend to co-locate with either the primary sensory/motor areas or the important multimodal association areas which integrate information from multiple areas. We also identified that age and sex did not significantly affect the properties of the cortical network on a global scale.

**Conclusion:** This study provides a baseline healthy-brain study of the human short association fibre connectome, and delivers vital methodological information surrounding SAF length which intends to improve the reliability and cross-comparability of SAF studies in the future. Our findings regarding regions of higher connectivity and integration concur with previous studies of the human connectome, and suggests that our method may also be sensitive to how different pathological connections, and therefore could be applied in a clinical context in future to investigate the role of SAF in neuropathology.

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**Acute innate immune responses to simulated transplantation surgery in two HD mouse model**

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**Aim:** Neurosurgeons have increasingly been involved in cell replacement therapy across the UK. Multiple studies provide proof-of-concept for the benefits of cell replacement therapy (CRT) in neurodegenerative diseases such as Parkinson’s and Huntington’s disease (HD). HD is a pathfinder condition for developing new treatments for neurodegenerative diseases. Its autosomal dominant inheritance with full penetrance, which allows for premorbid diagnosis and its focal striatal loss of a single population of medium spiny neurons make HD an ideal target for cell therapy and repair. Attaining a high survival rate of the cells post-transplantation has remained a significant challenge. Neuroinflammation is crucial in the onset and progression of HD. We hypothesise that inflammatory response to CRT surgery might be exacerbated due to a primed intrinsic inflammatory environment, partly explaining cell death and graft failure. This study aims to define innate immune responses to simulated transplantation surgery in two HD mouse models (HDQ175 and HDR6/1). 96 adult mice were used (24 HDQ175, 24 HDR6/1 and 48 wild-type control). Mice were either kept as Control (no surgery, time 0), or underwent bilateral stereotactic needle insertion to the striatum simulating CRT surgery and culled at 1 h, 24 h or 72 h post-surgery. A 3mm cube of tissue surrounding and including the injury site was collected for RNA sequencing and multiplex cytokine analysis. Analysis was performed using 2way ANOVA with Tukey’s tests, gene expression analysis was performed using Ingenuity Pathway Analysis. All animal experiments and surgical procedures were conducted under the UK Animals (Scientific Procedures) Act 1986, and subjected to local ethical review and relevant personal, project and institutional licenses.

**Results:** Simulation of the surgical aspect of cell replacement therapy through the introduction of a needle into HD brain produced an acute pro-inflammatory response, with IL-1B, IL-6, TNF-a and CXCL1 being raised at 1 h post needle insertion in HDQ175, model and at 1 h and 24 h in HDR6/1 model. RNA sequencing analysis and gene set enrichment analysis, confirmed upregulation in pro-inflammatory pathways including neuroinflammation signalling, NF-κB, Toll-Like receptor, IL-6, IL-17 and IL-33 signalling in both models. Other pathways which exhibited a response include complement activation pathway and HD signalling pathway.

**Conclusion:** The amplified pro-inflammatory response to needle injury in HD brain compared to wild-type, reveals a state of enhanced basal pro-inflammatory activation. Thus, the HD brain appears to be “primed” to produce an enhanced immune response. The inflammatory reaction to surgical trauma post-CRT is likely to contribute to neural graft site hostility. Simultaneous modulation of these pro-inflammatory pathways during graft delivery may improve graft survival in CRT and advance the translation of direct intraparenchymal delivery of cells into neurosurgical therapeutic practice. The concept of immune modulation in HD if successful, can then be rolled out to cell replacement therapy in other conditions such as Parkinson’s, Alzheimer’s and stroke.

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**An investigation into regional specific microglial gene expression and function in the control of hippocampal neural stem and progenitor cell regulation**

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**Aim:** Hippocampal neurogenesis is important for certain types of memory formation and processing. Additionally, there is an association between rates of hippocampal neurogenesis and brain disorders which is thought to underlie negative symptoms and cognitive decline in patient populations. Hippocampal neurogenesis therefore, is an attractive target to prevent and/or slow down memory decline. What regulates this neurogenic phenomenon within the dentate gyrus of the hippocampus remains unclear. Previously, our group has suggested a role for microglia, showing the addition of hippocampal microglia or microglia-conditioned media to cultured neural progenitor cells (NPC) has a positive neurogenic effect. Furthermore, recent studies have highlighted distinct regional transcriptional phenotypes of microglia, suggesting selective local functionality (Matcovitch-Natan et al. 2016). We hypothesise that differential neurogenic properties exist between microglia isolated from different brain regions which is likely underpinned by differential gene expression.
Method: Firstly, we have worked to determine whether reported site-specific interactions between microglia and NPC is maintained in vitro by looking at differential effects of microglia isolated from different brain regions including the DG and rest of the hippocampus from post-natal day 7–10 Sprague-Dawley rat pups. Microglia were expanded in mixed glial cultures and isolated by plate shaking. Once isolated microglia were either used directly on hippocampal NPC cultures or to generate microglia-conditioned media. The effect of applying microglia or their conditioned media to hippocampal NPC was examined by immunocytochemistry and fluorescent microscopy, inspecting markers for the cell cycle, neuronal stem cells and immature neurons. Secondly, we examined differential gene expression in mouse microglia isolated from the DG, rest of the hippocampus and cortex by performing bulk RNA-sequencing, followed by downstream analysis using DESeq2. Microglia were isolated using fluorescence activated cell sorting (FACS) and a P2RY12 positive selection.

Results: Our culture experiments showed that microglia or microglia-conditioned medium selectively increases NPC, but did not increase subsequent neurogenesis across all groups in this paradigm. We suspect specialist phenotypes of microglia are lost during in vitro culture. After performing RNA-sequencing, pair wise comparisons showed 1728 differential expressed genes between microglia isolated from the DG and rest of the hippocampus ($P < 0.001$). In comparison, only 38 differentially expressed genes were observed between microglia isolated from the DG and Cortex. GO term enrichment showed many significant terms of interest for the pair-wise comparison between DG and the rest of the hippocampus including neurogenesis and neuron differentiation.

Conclusion: In conclusion, microglia derived from the DG appear to show a significant differential gene expression compared to those isolated from the rest of the hippocampus. These differentially expressed genes may contribute to a functional, regional specific, neurogenic microglial phenotype within the DG and potentially contain good biological targets to undergo further investigation to prevent and/or slow down memory decline.

The ABC-ICH North of England project
H. Patel, M. Sutton, P. Wilson, M. James, L. Brunton and A. Parry-Jones

Aim: Intracerebral haemorrhage (ICH) is associated with significant morbidity and mortality. Through a quality improvement (QI) project, the “ABC” care bundle for ICH was developed, implemented and refined in Greater Manchester. This reduced 30-day deaths by one-third at Salford, saving two lives per month. The bundle consists of guideline-recommended interventions: Anticoagulant reversal, Intensive Blood pressure lowering and a Care pathway for prompt neurosurgical referral.

Method: A scale-up QI project across the North of England is now underway. Seven regional groups of stroke units in the North of England centred on their referring neurosurgical units (Preston, Walton Centre, Sheffield, Hull, Middlesbrough, Newcastle, Leeds) have been established. They will be supported by a Central Project Team, with meetings three months prior to launch and then three and six months after. The ABC-ICH app and dashboard will facilitate the project. Routinely collected Sentinel Stroke National Audit Programme data will be used to perform a service evaluation to determine changes in key care processes, case fatality, disability at six months and healthcare costs at sites before and after the project.

Results: The project commenced on Feb 2021. Sheffield and Middlesbrough have had their regional induction meetings with the remaining 5 regions planned at monthly intervals.

Conclusion: We will present an update on the project progress and share the “Manchester” protocol to help with wider engagement and to canvas wider opinions to inform the ongoing QI process.

COAST study – development of a core outcome set for cranioplasty following stroke or TBI
H. Mee, G. Whiting, P. Hutchinson and A. Kolas

Aim: In the first few days after a severe TBI or a large stroke, patients can develop pathological brain swelling, which, can lead to brain damage or death. Cranietomy is a surgical procedure in which part of the skull is removed to relieve the raised ICP attending to such brain swelling. Patients who survive eventually undergo a further operation, known as cranioplasty, to reconstruct their skull. With various studies being conducted, there is a growing interest regarding the optimal material, cost-effectiveness, and timing of cranioplasty concerning neurological recovery and possible complications. Consequently, heterogeneous reporting of outcomes from such diverse studies has led to a limited meta-analysis ability, with the ongoing risk of outcome reporting bias. One way to overcome these issues is to develop a “core outcome set” (COS), an agreed standardised set of outcomes that should be measured and reported, as a minimum, in the given health condition (1).

Method: An international steering committee has been formed to guide the development of the COS. In addition, recommendations from other clinical initiatives such as COMET (Core Outcomes and Effectiveness Trials) and OMERACT (Outcome Measures in Rheumatology) have been adhered to. The first phase of the project is data-collection through a systematic review and qualitative study. The second phase will be the COS-formation through a Delphi survey and consensus meeting. A definition of consensus will be decided and agreed upon before the Delphi survey begins to avoid bias, which is planned for the end of 2021.

Results: The phase 1 systematic review included a total of 205 studies. 202 verbatim outcomes were extracted, grouped into 50 domains and categorised into one or more of the OMERACT 2.0 framework core area(s). Total numbers of studies that reported outcomes in the core areas are: 192 (94%) pathophysiological manifestations/114 (56%) resource use/economic impact/94 (46%) life impact/mortality 20 (10%). In addition, there are 61 outcome measures used in the 205 studies across all domains.

Conclusion: The systematic review shows the considerable heterogeneity in the types of outcomes used across the cranioplasty literature. The core outcome set is being developed in conjunction with key stakeholder groups using robust, standardised, and transparent methodology. This iterative process focuses on ensuring a clear, non-bias pathway
for developing the COS. This research will help standardise outcome definition, collection, measurement, analysis, and interpretation in subsequent studies for cranioplasty. Finally, the continuing involvement of key stakeholder groups ensures the relevance of this research to all groups involved and, therefore, hopefully, makes it accepted as helpful research in the future.

**Automatic characterisation of the sylvian fissure morphology using a large neuroimaging dataset**

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**Exploring the clinical and host biological phenotype of neurosurgical patients who develop ventriculoperitoneal shunt complications**

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**Colloid cyst effects on both spatial neglect and memory before surgery and stable post-operative results**

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**Aim:** The multicentre randomised, single-blinded BASICS trial has provided level one evidence of the superiority of antibiotic impregnated catheters in preventing VP shunt infections. Post-hoc analysis has also demonstrated differential risk of both VP shunt infection and non-infective failure across age groups and aetiologies. We have developed a programme of proteomic and genomic analysis of banked CSF samples including those collected during the BASICS trial with the aim of identifying gene products differentially expressed in infected and non-infected in an attempt to identify potential biomarkers for the diagnosis or risk stratification of VP shunt infection.

**Method:** 223 samples from 200 patients representing a range of patient age groups and hydrocephalus aetiologies were cohornted. This number included 31 confirmed bacterial infections. These samples have undergone high throughput proteomic analysis at the Target Discovery Institute High Throughput Screening Facility, Oxford. A custom proteomic data analysis pathway has been developed utilising the open-source packages clusterProfiler, Limma and switchBox on the R statistical computing platform. This has been employed to identify gene enrichment patterns and provide gene functional annotation. In addition, existing data from a prior low-throughput proteomic run utilising a selection of the same CSF specimens has undergone the same analysis pathway to permit direct comparison of the techniques.

**Results:** High throughput proteomic analysis of CSF samples identified >1500 unique peptide signatures compared with 642 for the low throughput technique. A significant drop in sensitivity and resulting data quality was however noted for the high throughput technique. Linear modelling for differential gene expression between infected and non-infected samples followed by Top Scoring Pairs analysis has allowed identification of 135 potential candidate peptides relatively upregulated in infected cases (log fold change >0). Comparison across the 3 separate proteomic runs has allowed identification of 12 relatively upregulated peptides represented in at least 2 of the 3 proteomic runs. Functional annotation by Gene Ontology and KEGG databases has identified enrichment of a number of pathways of interest that are consistent across the 3 proteomic runs. These include humoral immune response, acute inflammatory response, complement and coagulation cascade and staphylococcus aureus infection.

**Conclusion:** Our proteomic analysis has demonstrated enrichment of a number of peptides involved in relevant functional pathways occurring in response to VP shunt infection. These peptides will be taken forward as candidate biomarkers for orthogonal ELISA validation. There is potential therefore to identify and develop a reliable marker which would enhance the diagnosis and management of VP shunt infection.

**Aim:** Colloid cysts are relatively uncommon, benign lesions, arising from the roof of the third ventricle, at or near the foramen of Monroe and the fornix. They can block cerebrospinal fluid outflow here causing obstructive hydrocephalus. Surgical excision aims to relieve these pressure effects. Post-operative memory impairment has been reported, thought to arise from effects on the fornix. We aim to explore whether colloid cysts are associated with other cognitive deficits, aside from memory.

**Method:** This is an exploratory sub-study of the CogENT study which prospectively used computerised cognitive testing for participants before and after resection surgery for brain tumours. The OCS-Bridge tablet computer based tool was used to deliver cognitive tests (1) across domains of attention, memory, perception, language, praxis and number cognition. The results were compared to normative data from a sample of healthy volunteers on the same electronic tests. Test results consistent with deficit were defined at 2SD from healthy normative scores, in keeping with the lowest 5-10% of those performances. For dimension and multi-collinearity effect reduction, the Line Bisection Test of pure spatial neglect (2) without memory encoding influence and Forwards Digit Span as a measure of pure verbal memory were analysed. Preoperative and postoperative MRI scans were used to calculate Evan’s Index as a surrogate marker for hydrocephalus. McNemar’s test and a multiple regression model were applied.

**Results:** 14 patients with Colloid cysts were recruited and assessed before surgery. 10 of these were also assessed after surgery. Only 2/14 patients had deficits in Forwards Digit Span before surgery compared to healthy normative data, whereas 6/14 had Line Bisection deficits suggestive of spatial inattention. Surgery was not associated with an exacerbation of these deficits; 1/10 retained a Forwards Digit Span deficit
Surgical team acceptability of brain computer interfaces in neurosurgery: a two-stage cross-sectional survey
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Aim: Brain-computer interfaces (BCI) detect neural activity and convert these signals into a coordinated output. Existing BCIs have been used to help with a range of functions including controlling computer programs, assisting rehabilitation, and controlling prosthetics. Invasive BCIs require neurosurgical implantation, thus carrying the risks of hospital admission, general anaesthetic, and a neurosurgical operation. Despite their promise, no existing studies have directly assessed the acceptability of these risks with the neurosurgical team. As key stakeholders in BCI technology, neurosurgeons are uniquely placed to quantify the risk versus benefits of BCI implantation. Here, we submit a work-in-progress proposal for a cross-sectional survey of the neurosurgical team to address these issues. This research aims to establish an understanding of the baseline knowledge of BCIs within the neurosurgical team, and subsequently to identify the attitudes of the neurosurgical team towards differing levels of BCI integration in neurosurgery.

Method: A two-stage cross-sectional international survey was conducted. The first, qualitative, survey assessed baseline understanding of BCIs, and will go live for two weeks in October 2021. Thematic analysis of results will guide generation of questions for second stage quantitative survey. The second, quantitative, survey will assess clinician acceptability of a range of BCIs and clinical applications, and will be conducted in November 2021. Participants will be asked to rank how comfortable they are with each BCI application, using a 5-point Likert scale (1 = least comfortable, 5 = most comfortable). Surveys will be distributed to neurosurgical units internationally, as well as via social media. Demographic data and participant role in the neurosurgical team will be collected. Surveys will be conducted using Google Forms. Statistical analysis will be conducted using SPSS.

Results: Results from both qualitative and quantitative surveys will be presented at the British National Research Group (BRNG) annual conference 2021. Expected outcomes include core themes regarding BCIs and considerations for the direction of future BCI research.

Conclusion: This proposed research will elucidate the wider opinions of the neurosurgical team with regards to acceptability of BCI.

POSTERS 1

A retrospective cohort analysis of ‘truly’ incidental low-grade gliomas
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A single centre experience in the management and outcome of low grade gliomas – a review of the literature and proposal of the Newcastle LGG Prognostication Calculator (NLPC)
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Approaches to lumbar decompression for spinal stenosis in the elderly – UK neurosurgeons’ attitudes and consideration of a surgical trial – LOFESS
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Computers on the brain: an exploration of machine learning in neuro-oncology
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Development of ‘Core Outcome Sets’ for meningioma in clinical studies: the COSMIC project
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eScooters – an evolving problem
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Factors influencing VP shunt failure: lessons from the BASICS trial
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Genome-wide association study of clinical outcome after aneurysmal subarachnoid haemorrhage
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Imaging timing after surgery for glioblastoma – an evaluation of practice in Great Britain (INTERVAL-GB)
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Paediatric lipomas with extraspinal extension – imaging and outcomes of a complex malformation
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Patient satisfaction with virtual spinal clinic appointments during the COVID pandemic, at the Great Western Hospital in Swindon
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Quality of online resources for traumatic brain injury patients and caregivers: time for reform?
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Safety and efficacy of dexamethasone in improving neurological outcomes in chronic subdural haematoma: a meta–analysis
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Safety and feasibility of posterior fossa neurosurgery in the supine position – a UK series from a large centre
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Seizure control in glioma related epilepsy: proposal of a qualitative attribute selection for a discrete choice experiment into patient priorities for treatment goals
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Serum amyloid-beta42 as a potential non-invasive biomarker for evaluating prognosis and histopathology of gliomas
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The demographics of patients with new brain metastases in the Southwest UK
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The effect of aging on presentation, management and outcomes in degenerative cervical myelopathy: a systematic review
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The feasibility of a medical student research elective to support data collection in the risk of aneurysm rupture study
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The global state of cranioplasty following cranial decompression for TBI: an international survey investigating local clinical practices and barriers to access
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The novel use of SecurAcath® for securing external ventricular drains in adults: a pilot study
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The role of In-Silico Clinical Trials (ISCT) in neurosurgery
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Three-dimensional printing in the armamentarium of the neurosurgeon: an overview of innovation
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