Rapid-Fire Session 1:

Functional Compensation in Moderate-Severe Paediatric Traumatic Brain Injury

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Introduction: The leading cause of disability in childhood and adolescence is moderate to severe traumatic brain injury (TBI; Langlois et al., 2006). Brain injury in childhood/adolescence can delay, disrupt or fundamentally alter ongoing brain maturation, resulting in poor long-term outcomes (Lindsey et al., 2018). Emerging evidence suggests that these outcomes are related to increased and decreased functional connectivity between brain regions. However, of the few studies that exist in this cohort, functional connectivity findings are inconsistent; which may be driven by the reliability of findings and functional MRI (fMRI) methods. In this study, we used independent component analysis (ICA) at the subject and group-level to inform ROI parcellations and reliably extract fMRI signal.

Method: 19 children with moderate-severe TBI (mean age 13.9 years ±3 years, 13 females) were compared with an age-matched control group of 20 children. A T1-weighted and resting-state fMRI scan (200 volumes) was acquired from each participant. Data were pre-processed using ANTs and FSL, before artefactual components were manually classified and regressed from fMRI data using single-subject ICA. Additional pre-processing steps were performed with SPM and Conn Toolbox. Group ICA was employed to inform ROI within the default mode network. Time-series were inspected in two ROI in each group, before post-hoc analysis of the amplitude of low frequency fluctuation was performed.
Results: Children with TBI showed increased functional connectivity between the posterior cingulate cortex and right lateral parietal cortex relative to controls as shown in fig 1 ($T(30) = 2.89$, $p = .03$ FDR corrected). In addition, increased FC was related to injury onset, whereby as recovery time increased, functional connectivity also increased. Finally, the TBI group showed a larger mean time series amplitude, however further analyses revealed no significant difference in amplitude of low frequency fluctuation.

Conclusion: Our findings suggest that young patients with TBI may be compensating for injury with increased right-lateralized parietal cortex functional connectivity. Our future analyses will examine whether this functional reorganization is associated with contralateral atrophy.

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Pathological slow-wave power is associated with post-traumatic amnesia following acute traumatic brain injury

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Post-traumatic amnesia (PTA) is a transient state of confusion following traumatic brain injury (TBI) characterised by inability to encode new memories. In healthy cognition, the successful formation of new memories requires increased theta and gamma power and reduced alpha.1 Higher delta:alpha power ratio (DAR) has been observed in patients with post-concussive symptoms2 and neurological outcome following moderate-severe TBI.3 Theta-gamma phase-amplitude coupling (PAC) is important in learning and memory4 and may be disrupted by the pathological low frequency oscillations seen in TBI. Resting state EEG recordings in 17 acute TBI patients and 21 healthy controls were acquired across 32 channels. PTA was assessed using the Westmead PTA scale and a neuropsychological battery was administered. We found i) PTA patients showed impairment relative to healthy controls across measures of associative working memory (WM), spatial short term memory, strategy search and attentional processing, but differed from acute TBI patients without PTA only on measures of associative WM. Acute TBI patients also showed attentional deficits compared to healthy controls. ii) increased low frequency power in patients disrupts WM. Specifically, PTA patients showed significantly increased DAR compared to TBI patients and controls which negatively correlated with measures of associative WM binding in all patients. iii) Theta phase synchronisation is significantly altered following acute TBI. Patients showed increased frontal-parietal theta connectivity which correlated with injury severity. iv) Theta-gamma PAC across frontal-parietal channels was significantly increased in patients compared to controls. Increased PAC was associated with attentional impairments but not with WM impairment. We have shown that PTA patients show a distinct neuropsychological profile from acute TBI patients not in PTA, and that this is associated with pathological low frequency oscillatory activity. We show evidence of abnormal connectivity within the fronto-parietal system in acute TBI patients through increased theta phase synchronsiation and theta-gamma coupling though this is non-specific to PTA. These novel results offer mechanistic insight into PTA and associative working memory deficit.

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Criticality and Complexity as a Diagnostic Approach for Patients with Disorders of Consciousness

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Introduction:
Disorders of Consciousness (DoC) describe patients that reside in a prolonged state of impaired awareness, commonly brought about by anoxic or traumatic brain injury (TBI). Classification of DoC patients' states of consciousness relies heavily on standardised measures that assess behavioural responses in a medical setting with limited diagnostic accuracy, likely attributable to strict dependence on subjective interpretations and the presumption that patients can show awareness behaviourally (e.g. Schnackers et al., 2009). Given the detrimental prognostic, ethical and social implications of DoC misdiagnosis, research has aimed to develop more objective diagnostic models. Accordingly, the current study examines promising computational models for DoC diagnosis within the frameworks of algorithmic complexity and criticality (e.g. Schartner et al., 2015; Fagerholm et al., 2015).

Methods:
Pre-collected data were analysed from 39 DoC patients, 18 of whom had suffered TBI before DoC onset (Bareham et al., 2019). Patients were examined for Coma Recovery Scale Revised (CRS-R) scores and EEG recordings for up to 8 follow-up assessments. The Lempel-Ziv complexity measure and the block decomposition method were assessed to gauge cortical algorithmic complexity. A neuronal avalanche, detrended fluctuation and phase lock interval analysis were conducted to examine state of criticality. Output measures were compared across patients in relation to assessed behavioural symptoms and CRS-R scores.

Provisional Results:
First results suggest complexity scores significantly correlate with patients' global CRSR-scores. Before the conference, further analyses will be done to compare results based on differential DoC diagnoses, TBI related cause and assessed physical symptoms. Criticality measures have been extracted, but are yet to be statistically examined.

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Early disruption of intrinsic connectivity networks following moderate-severe TBI associated with long-term outcome: a multi-centre study

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Introduction: Moderate-severe TBI patients typically experience long-term disabilities and an early biomarker of their severity is useful. Resting-state functional connectivity (FC) inform us on the intrinsic network function and thus, might help differentiate TBI patients who will develop good or bad outcomes.

Methods: We studied resting-state fMRI in 97 patients 2-4 weeks following injury across six centres with 75 controls matched in age. Several preprocessing steps were employed to reduce structured noise and diminish scan-site differences. We employed a dual regression analysis to study FC within resting state networks likely to be affected by TBI, namely the default mode network (DMN), frontoparietal networks (FPN) and the executive function network. FC within each network was compared in patients and control groups while regressing out gender and site. Peaks of the resting-state network's statistical maps were used to define the centre of 10-mm diameter spherical regions of interest. Mean FC of the networks of interest was subsequently extracted from these spheres for each participant. Spearman's correlation coefficient was calculated to assess the relationship between FC and Extended Glasgow Outcome Scale (GOSE) 6 months and 1-year following the injury

Results: FC within DMN and right FPN showed abnormalities 2-4 weeks following TBI. FC of precuneus/Posterior cingulum cortex (PCC) and left inferior parietal cortex within DMN was reduced in patients in comparison to controls. Within right FPN, patients showed an increase of FC in supramarginal and middle frontal cortex when compared to controls. Lower FC within DMN in patients was associated with lower GOSE at 6 months. Lower FC in inferior parietal cortex was also associated with lower GOSE at 12 months. In contrast, increased FC in supramarginal were significantly associated with higher GOSE at 6 months.

Conclusions:We have shown abnormalities in DMN and FPN early after moderate-severe TBI. These abnormalities correlate with the patient's outcome mainly at 6 months and may serve as an early biomarker for patient prognosis. Future studies will be needed to analyse the evolution of these abnormalities over time and provide insight into the pathophysiology/recovery following TBI. Inclusion of DTI data would also allow us to understand the relation between structural damage and changes in white matter over time with changes

in FC

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Introducing a new pipeline for diffusion imaging analysis: Subject-Specific Diffusion Segmentation

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Background: In the context of Traumatic Brain Injury (TBI) and other clinical investigation of WM abnormalities, diffusion magnetic resonance imaging (MRI) is widely used to investigate white matter (WM) microstructure (1, 2). The technique has proved extremely useful for determining brain structural connectivity as well as for the quantification of white matter abnormalities in a wide range of disorders (3-5). Region of Interest (ROI) approaches are used to focus analysis on particular WM tracts and these are often combined with voxel-based analyses carried out on images registered into a standard space (6). In individual space, ROIs are often drawn manually onto diffusion images. In contrast, automated voxel-based analysis rely on the combined analysis of diffusion images registered into group space (7). Both ROI and VBA-type analyses have well-established pitfalls: ROIs are often drawn manually onto diffusion images. This approach is time-consuming, requires specialist anatomical knowledge, and can be lead to biased estimation of diffusion metrics (7), while VBA are vulnerable to in accuracies introduced by the registration technique that may produce partial volume effects that are particularly problematic where white matter tracts are small or at the edges of larger tracts (8, 9).

Objective: Subject-Specific Diffusion Segmentation (SSDS) is a new validated pipeline carried out in native diffusion space. It relies on predefined anatomical regions in a template, back projected into individual diffusion parametric maps such as Fractional Anisotropy (FA). SSDS limits errors due to misalignments and smoothing while preserving the accuracy of the underlying anatomy. The pipeline involves limited manipulation of raw diffusion data, which excludes any need for smoothing or warping of the diffusion images for voxel-wise correspondence. It is fully automated, requires minimal intervention, and generates diffusion metrics with high reproducibility. It can be used to segment whole-brain WM maps, specific WM tracts, or any ROI based on a pre-existing atlas segmentation. Moreover, we eliminate any need for parameter changes, leading to a more homogenous methodology for easier reproducibility across clinical studies, which is an important limitation of DTI studies to date.

Methods: We test SSDS in a cohort of healthy subjects scanned three times, and investigate its performance in patients with Traumatic Brain Injury (TBI). FA maps are estimated from the raw DWI image, using common pre-processing methods. A set of registrations using the structural T1 image as mid-point enables back projections of the 47 tracts from the JHU white matter atlas to individual subject space. Mean FA, or histogram FA distribution can then be estimated for each tract across all subjects independently.

Results: The pipeline was validated on 17 subjects with healthy scans using test-retest measures and comparisons to other methods (group-level and manual segmentation). Coefficient of variation shows successful segmentation (COV < 5%) on 85% of tracts. Mean FA values obtained from manual segmentation and from SSDS were similar (p-value > 0.1). Case studies of TBI patients showed similar mean FA values using SSDS and manual segmentation.

Rapid-Fire Session 2:

Developing a mechanistic understanding of tDCS

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Introduction:
Transcranial direct current stimulation (tDCS) is a form of noninvasive brain stimulation that has been studied as a potential cognitive therapy. However, there is substantial variability in the effects tDCS, hindering its translation into routine clinical use. Previous work by our lab and others have found that brain state, stimulation polarity and white matter (WM) structure are independently important drivers of the effects of tDCS. This study aimed to investigate the combined influence of white matter structure, brain state and polarity on the effects of tDCS on brain networks.

Methods:
We used an experimental paradigm of simultaneous stimulation and fMRI acquisition to assess the effects of anodal or cathodal tDCS on two brain networks relevant to cognition. The salience network (SN) and the default mode network (DMN) display robust, reliable, anticorrelated network activity during the choice reaction task (CRT), which was used to manipulate brain state. Stimulation was directed to the right inferior frontal gyrus (rIFG) due to its key role in coordinating DMN and SN activity. Fractional Anisotropy (FA) was used as a measure of WM structure. We recruited 59 participants, consisting of healthy controls (n = 24; 12F:12M; mean age = 39 years, SD = 15.8 years) and traumatic brain injury (TBI) patients (n = 35; 5F:30M; mean age = 39.7 years, SD = 10.3 years).

Results:
We found that brain state and stimulation polarity were key parameters influencing the effects of tDCS on brain networks in TBI patients, replicating findings from our previous study in a different cohort. We compared the effects of tDCS on brain activity in TBI patients and healthy controls, and expected to see differences due to the impaired WM structure of TBI patients. Contrary to our hypothesis, we found no difference between the two groups. We then combined the two groups in our investigation of the influence WM structure exerts on the brain-state dependent effects of tDCS. In the absence of task increased FA correlates with increased activation of several DMN nodes. In these nodes, WM structure influences the effects of stimulation in the direction of the baseline set by brain state.

Conclusions:
Our results solidify the importance of brain state, stimulation polarity, and WM structures as parameters of tDCS. These parameters of tDCS and their interactions influence the physiological effects of stimulation.

Analysis of Head Impact Kinematics in Collegiate and Elite Women's Rugby Union

Freja J Petrie

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Women's participation in rugby union has seen unprecedented growth[1], yet current training and injury protocols are devised almost exclusively from male data[2]. Women are 2.6 times more likely to suffer mTBI in sports than men[3]. Non-scalable sex differences within axonal structures lower the accelerative tolerance of neuronal tissue[4]. Anatomical differences in the cervical spine minimise force attenuation as the stabilising musculature of the neck is comparatively weaker in women[5,6]. The generalisation of male-derived data is therefore limited and current recommendations of contact technique may not protect women from injury. This study sought to analyse female-specific kinematics of head impact events (HIEs)in elite and collegiate women's rugby union.

Video of women's matches was analysed to study the kinematics of direct and indirect HIEs. For elite players, two matches between four elite national teams were analysed and compared with collegiate matches. In the collegiate demographic (n=15)instrumented mouthguards (iMGs,ProtechtTM) were also used to quantify HIEs over six matches. The iMG system employed tight sensor-skull coupling, minimising soft tissue artefact and had undergone validation testing.

The iMG system recorded 130 video-verified HIEs in six collegiate matches. The average peak linear and rotational acceleration was 17g (SD 8.9, max 45 g) and 1305 rads/s2 (SD 1066, max 4292rad/s2)respectively. Most (49.2%)HIEs occurred as the head impacted 'hard' body parts. The second cause of HIEs was head-ground contact as the player fell, rather than during the contact phase as in the men's game. As the players fell, muscular control of the neck appeared limited, resulting in a high magnitude, whiplash motion of the head into the ground, seen in 17.4% of tackles. This lack of control could be a consequence of insufficient cervical muscle strength needed to stabilise the head. In the elite demographic, incidence of whiplash style HIEs was less, with the lowest incidence in teams with a higher world ranking (WR). Whiplash style HIEs were observed in 2.6%(1st WR),3.7%(2nd WR),4.3%(4th WR) and 6.3%(9th WR)of elite tackles respectively.

Overall, head impact kinematics in women differed to comparable studies in men. HIEs in collegiate women commonly occurred during a fall from a tackle rather than in the contact phase. Elite women generally had sufficient cervical control to minimise head-ground contact, which collegiate players did not. This research highlights a need for improved understanding of female head impact kinematics, without which mTBI incidence will remain unacceptably high.

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Neck Strength and Head Acceleration: The Effect of Neck Strength Training on Head Acceleration in Male University Rugby Union

Tom N Pennington

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INTRODUCTION:
Reports of mild traumatic brain injuries (mTBI) and longer-term neurocognitive deficits are increasing in rugby union [1]. Increasing neck strength has been reported to reduce head inertial loading during impact events; a 0.45kg increase in neck strength reduced the risk of sustaining an mTBI by 5% [2]. Vestibular and proprioceptive inputs mitigate head acceleration through neck muscle activation in the opposite and same directions as the perturbation respectively [3]. Neck strength training is therefore a potentially valuable addition to rugby S&C protocols to dampen resultant head acceleration during impacts. Both deep and superficial neck musculature need to be addressed to improve head-neck segmental stabilization [4]. The objective of this work was to implement and monitor a neck strength training program for university rugby athletes and investigate the relationship between neck strength and neck strength in rugby.

METHODS:
Maximum isometric neck strength data was collected from 27 male university players at the beginning of the season. Tests were repeated following 5 weeks of neck-specific training. A bespoke, isometric neck strength testing apparatus designed to facilitate repeatable measures (restricting accessory muscles) was used. Four 150kg load cells were used to measure neck strength in four directions; flexion, extension, left and right lateral flexion. Athletes were securely strapped to a bench in a supported kneeling position and exerted maximal force with their heads on load cells in each direction (randomized) for 3 seconds, with three repetitions for each direction. A neck strengthening program was then implemented, beginning with deep neck flexor activation and progressing to weighted resistance training. Linear (PLA) and rotational (PRA) head acceleration data were collected throughout the season using instrumented mouthguards (iMG).

RESULTS:
Pre-season testing showed average force values of 253 (54), 273 (58), 199 (62) and 201 (57) N for flexion, extension, left and right lateral flexion, respectively. After 5-weeks, these values improved 5.5%, 9%, 18.8% and 12.2% respectively. Paired t-tests for each direction showed significant improvements for all except extension ($p < 0.05$). A Pearson's correlation showed athletes with greater neck strength to have lower PRA values throughout the season ($p < 0.05$).

CONCLUSION:
This intervention was successful in improving isometric neck strength. Findings also suggest that increasing neck strength may be effective in reducing the head inertial load experienced during rugby matches.

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Consumer Testing of Bicycle Helmets

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Introduction: Current bicycle helmet standards do not include angular acceleration for certification even though it is known that it is the dominant cause of brain injury (Willinger et al. 2014). The objective of this study was to develop an improved test method, including oblique impacts, to evaluate helmets sold on the European market.

Methods: The study presents a novel method to preform consumer testing of bicycle helmets. Four physical tests were conducted, shock absorption with straight perpendicular impact and three oblique impact tests. Computer simulations were made to evaluate injury risk. In total, 26 conventional helmets and one airbag head protector sold on the European market were included.

Results: In 13 helmets a linear acceleration lower than 180 g were measured, which corresponds to a low risk of skull fracture (Mertz et al. 1997). The airbag head protector performed three times better than the conventional helmets (40 g vs. other helmets that were around 171 g). The simulations indicated that the strain in the grey matter of the brain during oblique impacts varied between helmets from 12% to 32%, where 26% corresponds to 50% risk for a concussion (Kleiven and Hardy 2002). In total three helmets and the airbag head protector got a result that was below the threshold for a 50% risk of concussion in all the three tests. In general, helmets equipped with systems aiming to reduce energy performed better than the others. But the fact that a helmet is fitted with rotational protection is no guarantee that it is a safe helmet. One of the helmets that comes out worst in the test has rotational protection system.

Conclusions: All helmets need to reduce rotational acceleration more effectively. A helmet that meets the current standards does not necessarily prevent concussion. It is important that, when consumers purchase safety equipment, they spend their money wisely. Consumer testing can greatly assist in this by informing prospective purchasers about the objective performance of alternative products. Consumer testing could also encourage helmet manufacturers to up their game and bring to market new helmet models that perform at least as well as the best existing models.

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Fluid flow shear stress activates ion channel mechanosensors in a novel glial scar in vitro model

Alexandre Trotier

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Introduction

Neuroprosthetic electrode implants have been under investigation for decades and have been proven to be safe and efficacious as therapeutic devices for multiple diseases of the central nervous system (CNS) including Parkinson's and Alzheimer's disease [1].

However, studies indicate that, in situ, neuronal recording capabilities and charge deliverance decrease with time in implanted electrode systems. This loss of function can be attributed in part to a chronic inflammatory reaction resulting from the micromechanical shear stress experienced during the micromotions of the neuroelectrode.

This mechanical trauma results in an adverse tissue response characterized by glial scar formation and electrode encapsulation [2], causing the signal strength to decrease and adjacent neurons to move away from the electrode as a result of the surrounding region of gliosis.

In this study, we aim to develop an in vitro model using fluid shear stress on neural cell populations to reproduce gliosis in vitro.

Materials and Methods

Using a parallel-plate flow chamber system, ventral mesencephalic (VM) mixed primary cells were exposed to a pressure-driven fluid flow allowing the application of a defined shear stress of 0.1 Pa for 4 or 6 hours, to reproduce the micromotion occurring at the implant/tissue interface.

The cells were then kept in culture for 14 days before being assessed for gliosis hallmarks. The morphology and protein expression of neurons and glial cells were quantified by image analysis. Chondroitin sulphate changes were quantified by immunocytochemistry. Custom protein arrays and western blots were used to detect the expression level of neuroinflammatory proteins and to monitor the changes of mechanoreceptors and glycosylation.

Results

Data have shown that the applied shear flow leads to astrocyte reactivity and an overall pro-inflammatory environment.

Indeed, oscillatory fluid flow stimulation has in all conditions significantly increased the GFAP protein expression but also the number and size of astrocyte cells (Figure 1A,B), along with inducing the upregulation of glycosaminoglycan deposition.

More importantly, it has been observed that the exposition to micromotion stimulation induce an increase in the expression of several mechanoreceptors, such as members of the PIEZO and transient receptor potential (TRP) ion channel families (Figure 1C).

Discussion

We have developed an in vitro model using parallel flow shear stress that reproduces the mechanical stress experience by neural populations at the neuro-electrode interface.

We envisage that this model will be a valuable tool for future researcher in developing anti-inflammatory and anti-gliosis biomaterial approaches.

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Regional characterization of the dynamic mechanical properties of human brain tissue by microindentation

Andrea Menichetti

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Introduction

Traumatic brain injuries (TBIs) are a relevant health concern and a major cause of mortality and lifelong disability. In the EU alone, 1.37 million TBIs and 56,000 TBI-related deaths are estimated annually [1], with the elderly population having the highest morbidity and mortality [2]. However, little is known about the mechanical properties of the human brain, especially at the high rates of deformation representative of TBI loading scenarios. To the best of the authors' knowledge, this is the first study on the characterization of mechanical properties of human brain tissue using micro-indentation under the largest applied strain (35%) and highest strain rate (10/s) in the literature.

Methods

10 human brains were collected from subjects between 64 and 94 years of age and tested within 4±1 days post mortem. A custom-built micro-indentation apparatus was used to characterize the hyper-viscoelastic mechanical properties of 12 different anatomical regions of the brain including cerebrum, cerebellum and brainstem (Fig.1a). On average 5 tests per region were performed, during which the tissue was indented by a 250 µm diameter probe up to 35% strain and at 10/s strain rate. All experiments were approved by the KU Leuven Medical Ethics committee. An inverse finite element (iFE) algorithm was used to fit a neo-Hookean based quasi-linear viscoelastic constitutive model to the experimentally measured force-time data [3]. The mean instantaneous shear modulus mu_0 was compared between the different regions by means of a linear mixed model with a random intercept for the brain specimen and for the region within the brain.

Results

The shear moduli were obtained from the combined iFE and parameter fitting algorithm from each test. As shown in Fig.1b, mu_0 varied across the regions: prefrontal cortex, superior mid-frontal cortex and cerebellum exhibited the lowest mean values (3.65±1.92 kPa, 3.53±1.27 kPa and 3.40±0.92 kPa, respectively), while corona radiata (7.63±2.01 kPa) and basal ganglia (7.62±3.04 kPa) the highest. Each region was statistically significantly different from at least one other region ($p<0.05$, data not shown). The influence of age, sex and time post mortem were also assessed, but within the tested cohort, none of these factors had a significant effect on the regional differences in terms of mu_0.

Conclusions

In this study, for the first time, the hyper-viscoelastic material properties of human brain tissue under large strain and high strain rates representative of TBIs were characterized by means of micro-indentation. These findings address the paucity of data in literature on human brain properties and highlight the differences across the different anatomical regions. Moreover, these results will improve the accuracy of results from 3D finite element models of the human head.

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Quantifying 3D in situ Brain Deformation During Dynamic Head Rotational Loading

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Introduction: Currently, finite element (FE) computer models of the human brain are the state-of-the-art technique for assessing brain injury risk, investigating potential TBI mechanisms, and developing preventative mechanisms [1]. These models allow researchers to simulate real-world head impacts to understand risk of injury and the efficacy of safety devices. However, more experimental brain deformation data at injurious impact conditions are needed to validate these models. The objective of this study was to measure 3D in-situ human brain deformation during high-rate rotational head motion at conditions considered injurious.

Methods: Using our previously developed in situ technique [2], six post-mortem human head-brain specimens were instrumented with an array of 32 neutrally-dense sonomicrometry crystals that were implanted into the brain (Figure 1). A dynamic rotation was then applied to the head using a closed-loop controlled test device. Four pulses with different severity level, ranging from a peak angular velocity of 20 – 40 rad/s with a duration of 30 – 60 ms, were applied about three orthogonal anatomical axes of rotation for a total of 12 test conditions per specimen. Dynamic 3D spatial time-history data for each crystal was calculated using time-of-flight data between crystal pairs, and processed using an extended Kalman filter trilateration algorithm [3] and reported as brain tissue displacement relative to the skull. A total of 72 tests were conducted for the six specimens, generating over 5000 displacement time-histories for use in computational model validation.

Results: Brain motion was direction-dependent, with axial rotation resulting in the largest magnitude of displacement (Figure 2). Peak-to-peak displacement amplitudes reached as high as 23 mm in the most severe case. The transient duration of the brain response lasted for 100-150 ms after the head rotation had stopped. Displacements were largest in the mid-cerebrum, and the inferior regions of the brain—the cerebellum and brainstem—experienced relatively lower peak displacements. Brain motion was also found to be positively correlated to peak angular velocity, and negatively correlated with angular velocity duration, a finding that has implications related to brain injury risk-assessment methods.

Conclusions: This is the first study to quantify 3D human brain deformation human in multiple specimens in response to varying severity rotations in all three anatomical planes. This data is made available for computational researchers to improve the biofidelity of their FE brain models. Ultimately, this dataset and test methodology will lead to better techniques for predicting and mitigating concussion risk.

High-fidelity finite element modelling of brain angioarchitecture for a rat model of TBI

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INTRODUCTION

Vascular damage is a key injury in the acute phase of TBI and a recent study has shown an association between vascular injury and patient's outcome after TBI [1]. However, it is still not understood how mechanical forces translate to vascular changes and aggravates secondary injury cascades. Here we incorporated detailed anatomy of vasculature in a high-fidelity Finite Element (FE) model of TBI in rats [2] to predict the distribution of mechanical forces across the vascular network and determine its association with the vessel's anatomy.

METHODS

We have developed a high-fidelity FE model of a rat brain tissue and its angioarchitecture based on high-resolution images acquired with synchrotron radiation phase contrast imaging (SR-PCI) technique [3] to simulate Controlled Cortical Impact (CCI). Our FE model was validated according to the lesion maps acquired from rats subjected to CCI, using the same parameters. We used our validated model to predict the stress wave propagation across the brain vasculature and investigate the interaction between stress wave within the brain tissue and vessels network.

An inhouse MATLAB code was used to generate a 3D FE model of the CSF, cerebrum, ventricles and vasculature. We modeled the brain tissue using solid elements and a visco-hyperelastic material model and the vasculature was modelled using beam elements and an elastic material model [4-5]. We used this model to simulate the CCI (Fig 1) and predict the distribution of mechanical forces in the vessels. We also developed microscale models of regions of interest to predict forces in capillaries.

RESULTS AND DISCUSSION

We found good agreement between the volume of the lesion and the volume of the brain exceeding a 35% strain threshold [2]. Both Lesion and strain maps showed larger injury near the edges of the impactor. We predicted large axial stresses in the ipsilateral cortical vessels, with maximal stresses being concentrated in vessels that are close to the edges of the impactor (Fig 2 - left). Interestingly, the cortical vessels directly under the impactor, which are mainly aligned with the direction of penetration, were not subjected to large forces. However, in the corpus callosum below the impacted cortex, where vessels are mainly running perpendicular to the direction of penetration, our model predicted large axial forces in the vessels. Using the microscale modelling, we predicted axial stresses in a small region containing a few capillaries (Fig 2 – middle and right). Our results show that axial forces vary significantly across individual capillaries that are few microns apart. This FE model allowed us to predict mechanical forces in vessels immediately after CCI and determine the interaction between the brain tissue, the anatomy of neurovasculature and stress distribution across scales. Our work shows that the vascular network can influence the stress distribution in the individual vessels and capillaries.