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BACKGROUND: Cerebellar mutism syndrome (CMS) is the commonest and most serious complication of posterior fossa tumour surgery with life-long consequences on speech and motor function. Despite previous identification of pre-operative clinical and radiological predictors of CMS, a unifying pre-operative risk stratification model for use during surgical consent is currently lacking. The aims of the project are to develop a simple pre-operative risk scoring scheme to stratify patients in terms of post-operative CMS risk. METHODS: Pre-operative radiological features were recorded for a retrospectively assembled cohort of 89 posterior fossa tumor patients from two major UK treatment centers (age 2-23yrs; gender 28M,61F; diagnosis: 38 pilocytic astrocytoma, 32 medulloblastoma, 12 ependymoma, 1 high grade glioma, 1 pilomyxoid astrocytoma, 1 atypical teratoid rhabdoid tumor, 1 hemangioma, 1 neurilemmoma, 2 oligodendroglioma). Twenty-six (29%) developed post-operative CMS. Based upon results from univariate analysis and C4.5 decision tree, stepwise logistic regression was used to develop the optimal model and generate risk scores. RESULTS: Univariate analysis identified five significant risks and C4.5 decision tree identified six predictors. The final model has an accuracy of 88.8% (79/89). Using risk score cut-off of 203 and 238 allowed discrimination into low (38/89, predicted CMS probability < 3%), intermediate (17/89, predicted CMS probability 3–52%) and high-risk (34/89, predicted CMS probability ≥ 52%). CONCLUSIONS: We will continue to work with leading neurosurgical centres in Europe and North America to expand the cohort and organise an international workshop in Nottingham to (1) validate and/or modify the preliminary model; (2) compare surgical techniques through detailed discussion; and (3) use the information exchange to establish a stratified approach to cerebellar mutism risk reduction. Following further multi-centre validation, this tool could be of value in providing CMS risk during the consent procedure and for stratifying patients in terms of CMS risk in trials of therapeutic strategies.

TRTH-25. REDUCING TIME TO DIAGNOSIS OF PAEDIATRIC BRAIN TUMOURS IN THE UK – HEADSMART AWARENESS CAMPAIGN (WWW.HEADSMART.ORG.UK)

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BACKGROUND: Public and professional concern about delays in diagnosis of childhood brain tumours has led to a clinical referral guidelines and the HeadSmart campaign to raise awareness of the early features of brain tumours and the need for timely imaging. As part of the outcome evaluation, we have collected data on total diagnostic intervals (TDI) i.e. intervals between symptom onset to diagnosis through a national service evaluation. The aims of the project are to (1) report the most recent TDI; and (2) identify the subgroup(s) with the longest symptom interval. METHODS: Paediatric brain tumour cases (aged 0–18 years) diagnosed between June 2014 and May 2015 were identified through a network of HeadSmart clinical champions. Age at diagnosis, dates of first symptom onset, first presentation to healthcare and diagnosis, tumour site, diagnosis were collected thorough an online data collection form. RESULTS: Data of 334 eligible cases, representing over 75% of incident cases in the UK of that year were recorded. TDI showed a right skewed distribution with a 90th percentile of 48 weeks and maximum of 313 weeks. Group median TDI had reduced significantly from 14.4 weeks in 2006, to 9.1 weeks in 2011 at the time HeadSmart was launched, and then to 6.5 weeks in 2015. Stratified analysis showed that there is still a significant difference between age groups. Median TDI is 3.9, 6.6 and 9.9 weeks for children under 5, 5–11 years and 12–18, respectively. CONCLUSIONS: These findings justifying a more targeted approach for the awareness campaign. With a rebranded website (www.headsmart.org.uk), new animation, posters to summarise symptom by subspecialty and quick reference guide, we hope to raise the awareness amongst young people aged 12–18 years and general practitioners, and reduce the median TDI further to national target of four weeks.

TRTH-27. A UK STUDY OF BLINDNESS CERTIFICATION RATES (2007–2011) IN YOUNG PEOPLE AGED 0–24, DIAGNOSED WITH BRAIN TUMOR: A POPULATION LINKAGE STUDY

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INTRODUCTION: Vision loss occurs in children with brain tumour due to prolonged pre-diagnostic raised intra-cranial pressure or by direct involvement of visual pathway structures. The HeadSmart campaign was launched in 2011 to disseminate national referral guidelines for brain tumor diagnosis, published in 2008 and demonstrated to be associated with a reduction in Total Diagnostic Interval (TDI) from 13.4 weeks in 2006 to 6.7 weeks in 2014. METHODS: Records of patients with brain tumor diagnosed aged 0–24 years from the National Cancer Registry (1997–2012, n = 19,555) were probabilistically linked to 13,013 national records of the electronic Certificate of Visual Impairment (eCVI, 2007–2012), to identify 336 brain tumor patients with registered partial or complete vision loss. Variation in the risk of vision loss associated with different tumor location and histology was estimated. In this cohort CNS neoplasm, optic atrophy and multiple causes accounted for 36%, 17.5% and 15.3%, respectively, of eCVI certifications. RESULTS: Overall, vision loss occurred in 3.7% of childhood brain tumor patients up to two years after diagnosis. The risk was greatest (6.0%) in 0–5 year-olds and lowest (1.5%) in 19–25 year-olds. Tumours above the tentorium (5.1%), cranial nerve (4.5%) and in the midline (4.2%) pose the highest risk. Pilocytic astrocytomas, choroid plexus tumors, sellar tumors, nerve sheath tumors and pineal tumors were also strongly associated with vision loss. eCVI registrations fell from 5.8% in 2007 to 3.5% in 2011. CONCLUSIONS: Brain tumour was the commonest cause of blindness certification, affecting 6% of children aged <5 years, it was most common in benign / slow growing tumors affecting midline structures. The proportion with blindness certification has fallen between 2007–2012, coinciding with the reduction in reported TDI since the launch of referral guideline, which was the focus of the subsequent HeadSmart campaign. Certifications data provided by the Certifications Office (The Royal College of Ophthalmologists, c/o Certifications Office, Moorfields Eye Hospital), captured by the Certificate of Vision impairment (CVI) are Department of Health copyright and this work was made possible by collaboration with the Royal College of Ophthalmologists. Any views expressed in the publication are those of the author(s) alone and not necessarily those of the Department of Health.

TRTH-28. HIGH THROUGHPUT SCREENING OF NOVEL HISTONE DEACETYLASE INHIBITORS FOR EPIGENETIC THERAPY OF PRIMARY BRAIN TUMORS

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BACKGROUND: Histone deacetylases (HDACs) are crucial regulators of epigenetic and posttranslational modifications and therefore represent a promising therapeutic target in cancer cells that harbor distinct epigenomes from normal cells. To exploit the therapeutic potential of HDAC inhibitors (HDACi) we synthesized a unique in-house library of more than 200 inhibitors. For the evaluation of the antitumor effects of the compound library in brain tumor cell lines, we successfully established an optimal screening workflow. METHODS: The screening procedure was streamlined by automated dispensing of cell lines, reagents and inhibitors using state of the art equipment. The drugs were evaluated for their effect on tumor cell viability in a panel of cell lines derived from different brain tumor entities (8 glioblastoma, 10 medulloblastoma and 6 atypical teratoid/rhabdoid tumor cell lines) and compared to 5 normal control tissues. Corresponding dose-response profiles were generated using an optimized bioinformatics workflow. In addition to our in-house library commercially available and clinically used HDACi (e.g. Vorinostat) were included. RESULTS: The semi-automated setup enabled the miniaturization of the assay format to 384-well plates. In combination with additional modifications, a remarkable increase of the overall throughput was realized, while generating accurate and reproducible results. Based on this workflow, we created a unique and comprehensive data set and could thereby identify various HDACi acting universally across brain tumors or being specifically active in distinct tumor