

#### QOL-15. NEURAL NETWORK INTEGRITY FOR FACIAL AFFECT RECOGNITION IN SURVIVORS OF MEDULLOBLASTOMA

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**BACKGROUND:** Medulloblastoma survivors are at risk for social deficits, yet underlying mechanisms are poorly understood. **METHODS:** Facial affect recognition was assessed in 50 medulloblastoma survivors treated with craniospinal radiation (median[range] 21.4[12.5–30.9] years old, 11.0[5.7–22.6] years since diagnosis) and 56 non-cancer age-, sex-, and race-matched controls. Brain activation and connectivity in core regions/nodes of the face perception network (fusiform gyri, occipital gyri, superior temporal sulcus) were examined using structural and functional neuroimaging. Structural networks were constructed from diffusion tensor imaging (DTI) data and individual node strength and efficiency were assessed. Functional MRI (fMRI) was conducted using a 1-back facial affect recognition task with assessment of regional differences in task-related cerebral blood flow (BOLD). Standardized neurocognitive testing was completed with 24 hours of brain imaging. **RESULTS:** Medulloblastoma survivors performed worse on a behavioral measure of facial affect recognition ( $P=0.003$ ) compared to matched controls. During the facial affect recognition task, controls demonstrated greater BOLD activation of the left and right fusiform gyri and the left and right middle occipital gyri compared to survivors ( $P's < 0.05$ , corrected for multiple comparisons). DTI indicated weaker core node strength in survivors in the right lateral occipital gyri ( $P=0.02$ ) and efficiency was lower in the left ( $P=0.01$ ) and right ( $P=0.03$ ) occipital gyri compared to controls. **CONCLUSIONS:** Medulloblastoma survivors have deficits in facial affect recognition and reduced activation and efficiency in brain regions comprising the face perception network compared to matched controls. Interventions targeting this specific skill and neural network may improve social functioning in survivors.

#### QOL-17. BIOLOGICAL CORRELATES OF QUALITY OF SURVIVAL AND NEUROCOGNITIVE OUTCOMES IN MEDULLOBLASTOMA; A META-ANALYSIS OF THE SIOP-UKCCSG-PNET3 AND HIT-SIOP-PNET4 TRIALS

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Relationships between biological factors (genetic, tumour molecular subgroup) and neurocognitive/Quality of Survival (QoS) outcomes in medulloblastoma survivors are emerging, based on studies of limited retrospective cohorts. Integrated investigations of the medulloblastoma late-effects pathway (considering biological, clinical and treatment factors), using larger clinically-controlled cohorts, are now essential to determine their independent significance and potential for clinical application. In a combined cohort of SIOP-UKCCSG-PNET3 and HIT-SIOP-PNET4 patients (n=150), molecular subgroup (MB<sub>WNT</sub>, MB<sub>SHH</sub>, MB<sub>Grp3</sub>, MB<sub>Grp4</sub>) was assessed against QoS measures [health status: HUI3; emotional and behavioural difficulties: SDQ; Health-related Quality of Life (HrQoL): PedsQL]. Additionally, in DNA remaining from HIT-SIOP-PNET4 (n=74), 39 candidate SNPs (involved in metabolism, DNA maintenance/repair, neural growth/repair and oxidative stress/inflammation) were genotyped by multiplexed MALDI-TOF MassArray and assessed against Wechsler Intelligence Scale (WISC) scores. Molecular subgroup was significantly associated with HrQoL and health status in univariate analyses; MB<sub>Grp4</sub> predicted significantly worse outcomes than MB<sub>SHH</sub> and MB<sub>Grp3</sub> ( $p < 0.05$ ), but not in multivariate analyses taking into consideration other significant and reported QoS predictors (e.g. treatment, gender, age). In contrast, 6 SNPs were significantly associated with  $\geq 1$  WISC domain; 4/6 showed associations across domains. 3 SNPs were independently prognostic in multivariate analyses, and further significant associations were apparent at the gene (*BDNF*, *APOE*) and pathway (folate) level. This cross-discipline, international study encompassing two medulloblastoma trials has identified relationships between molecular subgroup, genotype and survivorship outcomes. These findings now require assessment in larger series, to inform our understanding of medulloblastoma survivorship outcomes and impact future disease management strategies.

#### QOL-18. A LONGITUDINAL STUDY OF NEUROCOGNITION IN CHILDREN TREATED FOR A BRAIN TUMOR

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It is well known that neurocognition in children treated for a brain tumor can be affected. However, studies on the trajectory of these neurocognitive problems are scarce. In the present study we investigated the evolution of neurocognition between timepoints of diagnosis, 2, 4 and 6 years later. A total of 53 children diagnosed with a brain tumor were recruited in this study, of which all completed a comprehensive neuropsychological test battery at three successive timepoints and 30 at 4 timepoints. The first assessment was conducted as soon as possible after diagnosis and before initiation of chemo- and/or radiotherapy. Mean age at diagnosis was 8.06 years. The most common diagnoses were pilocytic astrocytoma (n=28) and medulloblastoma (n=10). 24.5% and 18.9% of these patient groups received focal or craniospinal irradiation, respectively. A repeated measures analysis with cranial irradiation (no, focal, craniospinal) as between-subjects factor demonstrated a significant interaction effect between time and type of irradiation for overall intelligence ( $p=0.02$ ) for children with three assessments. The same interaction effect was found for overall intelligence and processing speed for children with four assessments ( $p=.005$  and  $p=.002$ , respectively). The group who received craniospinal irradiation demonstrated the most pronounced decline. Interestingly, no main time effect or interaction effect was found for general memory functioning. Our results demonstrate that not all neurocognitive functions in children treated for a brain tumor decline after treatment. Overall IQ and processing speed are the most vulnerable outcomes in our cohort, especially for the children treated with craniospinal irradiation.

#### QOL-19. PARENT-REPORTED COGNITIVE PROBLEMS AND DIRECT ASSESSMENT OF COGNITION IN CHILDREN TREATED FOR A BRAIN TUMOR

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The Pediatric Perceived Cognitive Function (PedsPCF) item bank is a short parent and self-reported cognitive screening questionnaire developed in the context of pediatric oncology. The PedsPCF demonstrated satisfactory psychometric properties and the scores of the PedsPCF are found to be associated with clinical outcomes. Today little research is available to evaluate whether the PedsPCF is correlated with direct assessments of neurocognitive domains. The aim of the current study is to investigate whether important cognitive domains, such as different aspects of intelligence, memory, visuo-motor integration can predict the PedsPCF score. We obtained 100 PedsPCF filled in by parents from children treated for a brain tumor. All these children completed a comprehensive neuropsychological battery. Mean age at diagnosis was 7.47 years and mean age at completion of PedsPCF and testing 13.84. The most common diagnoses were pilocytic astrocytoma (n=43) and medulloblastoma (n=14). A linear regression model with verbal comprehension, perceptual reasoning, processing speed, visuo-motor integration as predictors for overall PedsPCF score was significant ( $p.005$ ), but the overall model fit was limited (adjusted  $R^2$ : 14%). Visuo-motor integration and processing speed were significant predictors (beta = 0.56 and -0.29). Our results are in line with the overall finding that the correlation between questionnaires assessing quality of survival and direct assessments of cognition are low. For clinical practice these results are important as the PedsPCF can't be used to replace direct cognitive assessments or vice versa.

#### QOL-20. IMPACT OF RADIATION DOSE AND VOLUME ON MEMORY FUNCTIONING IN CHILDREN WITH MEDULLOBLASTOMA: A REPORT FROM CHILDREN'S ONCOLOGY GROUP (COG) ACNS0331

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**BACKGROUND/OBJECTIVES:** We examined longitudinal verbal and visual memory functioning in children treated for medulloblastoma on COG protocol ACNS0331. **METHODS:** Children with medulloblastoma participated in neuropsychological testing at three timepoints over a 6-year period. Children aged 3–7 years were randomized to receive craniospinal irradiation.

ation (CSI) of either 23.4Gy (standard dose; SDCSI) or 18Gy (lower dose; LDCSI). Children aged 8+ received SDCSI. All children were also randomized to receive either a reduced radiation boost to the involved field (IFRT) or a standard boost to the whole posterior fossa (PFRT). Memory functioning was evaluated an average of 0.67(T1), 2.95(T2), and 4.90(T3) years post-diagnosis. RESULTS: Of 464 eligible patients enrolled on ACNS0331, 354 (76%; 65.3% male, 83.1% white) completed some neuropsychological testing. Mean age at diagnosis was 9.1 years (range=3–19). Verbal and visual short-term memory and learning were broadly within the average range for the overall sample at all three timepoints. However, a large percentage of children exhibited scores  $\geq 1SD$  below the mean on tasks of verbal learning both immediately (43.4%) and after a delay (40.7%) at T3. In addition, 58.6% of children randomized to SDCSI exhibited impairment in verbal learning after a delay compared to 34.8% of children randomized to LDSCI, and 35.0% of those aged  $\geq 8$  at diagnosis receiving SDCSI. CONCLUSIONS: Younger children receiving SDCSI have particularly high rates of memory impairment five years after diagnosis of medulloblastoma. Limiting CSI dose and/or volume in young children treated for this diagnosis may improve outcomes for memory functioning.

#### QOL-21. DEVELOPMENT AND UTILISATION OF A NEURO-ONCOLOGY REHABILITATION TEAM: 2018–2019 UPDATE

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INTRODUCTION: A multi-disciplinary Neuro-Oncology Rehabilitation Team (NORT) was established at our institution in 2014. We reviewed NORT inputs, processes and outputs in 2018 to 2019 compared to our previously presented data from 2015, soon after service inception. METHODS: Retrospective analysis of patients who received NORT input June 2018 - May 2019 compared to 2015 data. Descriptive analysis of changes to NORT operational processes and structure. Complexity of rehabilitation needs was measured using the Rehabilitation Complexity Scale-Extended V13 (RCS). RESULTS: 54 children received NORT input in 2018–2019 (10 children in 2015) with total of 129 outputs. NORT input was highest in children with high grade glioma (median reviews: 3; median RCS: 5) and ependymoma (median reviews: 3; median RCS: 5). Pilocytic astrocytoma formed the largest tumour group ( $n = 11$ ; median reviews: 2; median RCS: 7). 11% patients were referred to neurologist (9% already known); 17% referred to community services (44% already known); 31% referred to neuropsychology. In 2015, outputs were predominantly referral to occupational therapy and physiotherapy. 6 patients (11% of 54) were discharged in 2018–2019 (40% of 10 patients in 2015). 4 patients died. Between 2015 and 2019, developments included: clarifying referral and discharge pathways, use of screening measures, neuropsychology integration, therapy-led drop-in clinics, use of RCS-E. DISCUSSION: There has been a clear increase in utilisation and scope of work of NORT over last 4 years. The strength of this team is multidisciplinary working and expertise. Further developments planned: multidisciplinary rehabilitation interventions and NORT outcome tools.

#### QOL-22. MACHINE-LEARNING INFERENCE MAY PREDICT QUALITY OF LIFE SUBGROUPS OF ADAMANTINOMATOUS CRANIOPHARYNGIOMA

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BACKGROUND: Due to disease and/or treatment-related injury, such as hypothalamic, visual, and endocrine damage, quality of life (QoL) scores after childhood-onset Adamantinomatous Craniopharyngioma (ACP) are among the lowest of all pediatric brain tumors. Decision-making regarding management would be aided by more complete understanding of a patients likely QoL trajectory following intervention. METHODS We retrospectively analyzed caregiver and patient-reported QoL-instruments from the first 50 patients (ages 1–17 years at diagnosis) enrolled in the international Advancing Treatment for Pediatric Craniopharyngioma (ATPC) consortium. Surveys included 205 pediatric-relevant questions and were completed at diagnosis, and 1- and 12-months following diagnosis. Using Multiple Correspondence Analysis (MCA), these categorical QoL surveys were interrogated to identify time-dependent patient subgroups. Additionally, custom deep learning classifiers were developed using Google's TensorFlow framework. RESULTS By representing QoL data in the reduced dimensionality of MCA-space, we identified QoL subgroups that either improved or declined over time. We assessed differential trends in QoL responses to identify variables that were subgroup specific (Kolmogorov-Smirnov  $p$ -value  $< 0.1$ ;  $n=20$ ). Additionally, our optimized deep learning classifier achieved a mean 5-fold cross-validation area under precision-recall curve  $> 0.99$  when classifying QoL subgroups at 12 month follow-up, using only baseline data. CONCLUSIONS: This work demonstrates the existence of time-dependent QoL-based ACP subgroups that can be inferred at time-of-diagnosis via machine learning analyses of baseline survey responses. The ability to predict an ACP patient's QoL trajectory affords caregivers valuable information that can be leveraged to maximize that patient's psychosocial state and therefore improve overall therapy.

#### QOL-23. ASSESSING THE IMPACT OF METHYLPHENIDATE ON LATE COGNITIVE EFFECTS IN PAEDIATRIC BRAIN TUMOUR SURVIVORS: A SERVICE-BASED EVALUATION

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OBJECTIVE: One of the most disabling side effects of treatment in survivors of brain tumours is the resultant reduction in level of processing speed and attention. This study aimed to evaluate intellectual and psychological benefit of short-acting methylphenidate to survivors of brain tumour. METHODS: Paediatric BT patients attending a UK specialist treatment centre received assessment of cognitive performance. All patients identified with attentional difficulties were screened for contraindications to methylphenidate. Participants ( $N=23$ ), mean age 11.09 years, completed a 6-month trial of methylphenidate. Measures of attention (Test of Everyday Attention for Children 2; SNAP-IV), side-effects (Stimulant Side-Effects Rating Scale), Health-Related Quality of Life (PEDS-QL), and experience of methylphenidate questionnaire (purpose-developed semi-structured questionnaire) were administered prior to medication and after six months. RESULTS: Participants showed improvement in selective attention ( $t(18)=-5.4$ ,  $p<.001$ ,  $d=.93$ ) and processing speed ( $t(16)=-3.0$ ,  $p=.01$ ) at follow up. Family ratings of attention were significant ( $t(17)=14.46$ ,  $p<.001$ ,  $d=-1.19$ ). Change in subjective measures of Health-Related Quality of Life (HRQoL) was also statistically significant as reported by children ( $t(16)=3.91$ ,  $p=.001$ ,  $d=-.99$ ), and on a parental-report measure of child HRQoL ( $t(15)=-8.19$ ,  $p<.001$ ,  $d=-1.09$ ). HRQoL measures show improvement to physical, academic, and emotional domains as reported by participants. CONCLUSIONS: Paediatric BT survivors showed benefit from provision of methylphenidate in terms of reduced attentional and processing deficit, and in terms of emotional wellbeing. Treatment was well tolerated. Continued follow-up of the current participants in a longitudinal study aims to evidence longer-term benefit to participants.

#### QOL-24. DIFFERENTIAL IMPACT OF TUMOR LOCATION, LOCAL AND CRANIOSPINAL IRRADIATION ON NEUROPSYCHOLOGICAL LONG-TERM OUTCOME IN CHILDREN WITH MEDULLOBLASTOMA, EPENDYMOMA AND SUPRATENTORIAL PNET: A LONGITUDINAL MULTICENTER OUTCOME ASSESSMENT OF CHILDREN FROM THE HIT-2000 AND HIT-REZ TRIALS

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