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_{WNT}, MB_{SHH}, MB_{Grp3}, MB_{Grp4}) 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_{Grp4} predicted significantly worse outcomes than MB_{SHH} and MB_{Grp3} ($p<0.05$), 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 ≥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, visuomotor 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, visuomotor integration as predictors for overall PedsPCF score was significant (p.005), but the overall model fit was limited (adjusted R^2: 14%). Visuomotor 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 irradi-