Comparison of neuropsychological and brain imaging data in pediatric brain tumor patients surviving more than 10 years

Tonning Olsson, Ingrid; Perrin, Sean; Björkman-Burtscher, Isabella; Lundgren, Johan; Kahn, Anna; Johanson, Aki

Published in:
Neuro-Oncology

DOI:
10.1093/neuonc/nou076

2014

Link to publication

Citation for published version (APA):

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

• Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
• You may not further distribute the material or use it for any profit-making activity or commercial gain
• You may freely distribute the URL identifying the publication in the public portal

Take down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.
NP-001. INTRUSION INTO SELF-PERCEPTION BY CNS TUMOR AND TREATMENT IN CHILDHOOD OR ADOLESCENCE: POPULATION-BASED OUTCOMES FROM ADULT SURVIVORS EARLY CITED WILL IN GENERAL POPULATION
Kristër K. Roman1, Linda Hörnquist1, Jenny Rickhardsson1, Birgitta Lannerling2, and Goran Gustafsson1; 1Karolinska Institutet, Childhood Cancer Research Unit, Stockholm, Sweden; 2Stockholm University, Department of Psychology, Stockholm, Sweden; 3University of Gothenburg, Department of Clinical Sciences, Gothenburg, Sweden

BACKGROUND: Survivors of pediatric central nervous system (CNS) tumors at risk for persistent tumor/p其 treatment-related morbidity, disability and social consequences which may intrude into self-perception, vital for mental health and quality of life. Within the longitudinal Swedish CNS tumor LIFE-study, we studied the long-term impact of the childhood CNS tumor and its treatment on self-perception in significant domains in adult survivors, by comparing outcomes with those of the general population. METHODS: The cohort included 697 Swedish survivors diagnosed between 1982 and 2001 with a primary CNS tumor. Comparison data were collected from a stratified general population random sample. Survivors and general population individuals were matched according to gender, age and in the global self-perception index, compared with those from the general population (all P < 0.001). Within the survivor group, female gender and persistent visible physical appearance sequelae predicted poorer outcomes in several of studied domains. CONCLUSION: Intrusion into self-perception appears as a potential long-term psychological late effect in adult survivors after pediatric CNS tumors and the brain tumor treatment. Because of this risk, patient care and psychosocial follow-up should include measures similar to what was used in this study. Paying attention to self-perception within the global self-perception index appears in line with, or was significantly above, that expected on the basis of FSIQ. Most of these children had benign tumours treated with surgical resection only. CONCLUSIONS: These results suggest that early injury to the cerebellum has a generic effect on cognitive processing that underpins development of scholastic skills. Additional academic difficulties are likely to occur in children with invasive tumours requiring more aggressive treatment probably because chemotherapy and radiotherapy are known to affect attentional processing which is critical for scholastic progression.

NP-002. DO SCHOLASTIC DIFFICULTIES IN CHILDREN WITH EARLY CEREBELLAR MEDULLOBLASTOMA AND WORKING MEMORY DISORDERS: A FUNCTIONAL MRI STUDY
Duc Ha Hoang1, Anne Pagnier2, Emilie Cousin2, Karine Guichardet3, Isabelle Schiff2, Fanny Dubois-Tekali2, and Alexandre Kranz3; 1Granet Institute of Neurosciences, Grenoble, France; 2Department of Pediatrics - Grenoble University Hospital, Grenoble, France; 3Laboratory of Psychology and Neuropsychognition - University Pierre Mendès, Grenoble, France

BACKGROUND AND PURPOSE: Medulloblastomas are the most common malignant brain tumors in childhood. Children treated for a cerebellar medulloblastoma demonstrated cognitive disorders in working memory (WM), especially visuospatial WM, leading to an impairment of school performance. The purpose of this study is to describe the cerebellar involvement in specific cognitive deficits observed in children treated for cerebellar medulloblastoma. MATERIALS AND METHODS: Groups: Nine healthy volunteers (11.1 ± 2.2 yo), were compared to 5 patients treated for cerebellar medulloblastoma (12.1 ± 0.6 yo). All subjects were native French speakers, right-handed, with a global IQ of 70-130. Using 4 block-design 1-back tasks in the sensorial modality (visual/auditory) and the nature of information (verbal/nonverbal) during fMRI acquisitions (T2* weighted gradient-echo - EPI) and completing with an anatomic acquisitions (3D FI-weighted). Data Analysis: Using the Statistical Parametric Mapping (SPM8) and the Spatially Unbiased Infra-tentorial Template (SUIT) for viewing cerebellar topography with BOLD activations. RESULTS: In patients group: 4/5 patients had a WM deficit following a resection of the left posterior cerebellar lobe (lobule HVIII, HVI, I and II) and inferior part of vermis; the only patient without WM deficit was the only one without cerebellar hemispheric resection (figure 1), even though this patient was also treated with radiotherapy and chemotherapy dosages like those in other patients. Greater BOLD activations were found in the left posterior cerebellar lobe for nonverbal vs. verbal contrast and they were presented in this region for visual vs. auditory contrast (figure 2). In healthy subject, greater BOLD activations were found in brain and cerebellar locations which are similar with those in the literature for all four tasks. CONCLUSION: The cerebellum plays the same role in WM in children as that has been previously described in adults. The left posterior cerebellar lobe may involve the visuospatial WM.

NP-003. CHILDREN WITH CEREBELLAR MEDULLOBLASTOMA AND WORKING MEMORY DISORDERS: A FUNCTIONAL MRI STUDY
Duc Ha Hoang1, Anne Pagnier2, Emilie Cousin2, Karine Guichardet3, Isabelle Schiff2, Fanny Dubois-Tekali2, and Alexandre Kranz3; 1Granet Institute of Neurosciences, Grenoble, France; 2Department of Pediatrics - Grenoble University Hospital, Grenoble, France; 3Laboratory of Psychology and Neuropsychognition - University Pierre Mendès, Grenoble, France

BACKGROUND AND PURPOSE: Medulloblastomas are the most common malignant brain tumors in childhood. Children treated for a cerebellar medulloblastoma demonstrated cognitive disorders in working memory (WM), especially visuospatial WM, leading to an impairment of school performance. The purpose of this study is to describe the cerebellar involvement in specific cognitive deficits observed in children treated for cerebellar medulloblastoma. MATERIALS AND METHODS: Groups: Nine healthy volunteers (11.1 ± 2.2 yo), were compared to 5 patients treated for cerebellar medulloblastoma (12.1 ± 0.6 yo). All subjects were native French speakers, right-handed, with a global IQ of 70-130. Using 4 block-design 1-back tasks in the sensorial modality (visual/auditory) and the nature of information (verbal/nonverbal) during fMRI acquisitions (T2* weighted gradient-echo - EPI) and completing with an anatomic acquisitions (3D FI-weighted). Data Analysis: Using the Statistical Parametric Mapping (SPM8) and the Spatially Unbiased Infra-tentorial Template (SUIT) for viewing cerebellar topography with BOLD activations. RESULTS: In patients group: 4/5 patients had a WM deficit following a resection of the left posterior cerebellar lobe (lobule HVIII, HVI, I and II) and inferior part of vermis; the only patient without WM deficit was the only one without cerebellar hemispheric resection (figure 1), even though this patient was also treated with radiotherapy and chemotherapy dosages like those in other patients. Greater BOLD activations were found in the left posterior cerebellar lobe for nonverbal vs. verbal contrast and they were presented in this region for visual vs. auditory contrast (figure 2). In healthy subject, greater BOLD activations were found in brain and cerebellar locations which are similar with those in the literature for all four tasks. CONCLUSION: The cerebellum plays the same role in WM in children as that has been previously described in adults. The left posterior cerebellar lobe may involve the visuospatial WM.

NP-004. THE EFFICACY OF COMPUTERIZED COGNITIVE REHABILITATION TRAINING IN THE CHILD TREATED FOR MEDULLOBLASTOMA
Martina Bürger Lazari1 and Karmen Resnik2; 1University Medical Centre Ljubljana, Division of Paediatrics, Department of Oncology and Haematology, Ljubljana, Slovenia; 2University Medical Centre Ljubljana, Division of Internal Medicine, Department of Vascular Diseases, Ljubljana, Slovenia

OBJECTIVES: Neurocognitive deficits are common after brain tumor treatments. Our study suggests that computer-based means of rehabilitation lead to better cognitive functioning. Thus there is a need to include cognitive rehabilitation in a standard protocol. The present single case study evaluates the improvement of general cognitive functioning, focusing on the patient who underwent rehabilitation program targeting memory, alertness and attention. METHODS: The pediatric patient (age 7.5) diagnosed with medulloblastoma underwent surgery, craniopinal irradiation (23.4 Gy, with additional boost to the tumor site), chemotherapy (Altemi and Vincristin, Cisplatin), in 6 weeks intervals. Postoperative MRI did not reveal any tumor remnant. Neuropsychological tests (WISC III, CCT, CICT) showed below average performance in all areas of cognitive functioning. He started CogniPlus computer training targeting alertness (ALERT), mental rotation (ROTATE), working memory (VISP, NACK, DATEUP), and attention (SELECT, FOCUS, SPACE). He participated in 35 rehabilitation sessions (11 hours). After a year, the neuropsychological battery was repeated. RESULTS: Regression analysis revealed significant improvements in alertness, mental rotation, visuospatial working memory,
NP-005. COMPARISON OF NEUROPSYCHOLOGICAL AND BRAIN IMAGING DATA IN PEDIATRIC BRAIN TUMOR PATIENTS SURVIVING MORE THAN 10 YEARS

Ingrid Tonnigh Olson1, Sean Perin1, Isabella Björkman Bartsch2, Johan Landgren3, Anna Ke-Khalil2, Aki Johanson1; 1Department of Psychology, Lund University, Lund, Sweden; 2Department of Clinical Sciences, Lund University, Lund, Sweden; 3Skåne University Hospital, Department of Paediatrics, Lund, Sweden; 4Department of Psychology, Institute of Psychiatry, King’s college, London, UK

AIM: To explore the relationship between neuropsychological outcome and magnetic resonance imaging (MRI) findings in pediatric brain tumor patients surviving more than 10 years.

BACKGROUND: Cognitive late sequelae after pediatric brain tumour have a multifactorial origin. Low age at diagnosis, cranial radiation therapy, intrathecal methotrexate treatment and increased intracranial pressure are known to predict cognitive sequelae. Cognitive sequelae have been related to MRI findings, but the relation between neuroimaging findings and neuropsychological impairment needs to be explored further. METHOD: Sixteen pediatric brain tumor survivors completed an extensive neuropsychological test battery and MRI 10 to 13 years after diagnosis. Patients were first separately classified as positive or negative regarding neuropsychological impairment and MRI findings and then coded as congruent or incongruent, depending on whether neuropsychological outcome was in agreement with MRI also considering clinical data such as type and location of the brain tumour, post-operative status; treatments or premorbidity. RESULTS: Ten patients were classified as either positive or negative for both MRI and cognitive impairment if blinded for the second parameter and clinical data, and were also congruent for these two parameters when not blinded for clinical data and the second parameter. In five out of six initially incongruent patients the neuropsychological profile was in accordance with MRI findings when evaluating all data with the multidisciplinary holistic approach. CONCLUSIONS: Cognitive outcome in survivors of paediatric brain tumours depends on many different detrimental processes and shows high individual variation. Congruity between neuropsychological impairment and MRI findings might at first seem low. However, in the perspective of a clinical holistic evaluation of MRI findings and neuropsychological outcome considering the knowledge of clinical data such as type and location of the brain tumour, type of MRI findings (atrophy, gliosis, post-operative lesion), undergone treatments and radiation field as well as premorbid cognitive functioning is insufficient. Their specific cognitive and emotional functioning is the cause of non-standard results. For example some scales based on sense of humor and understanding of the absurdities are difficult to understand for patients with effective syndromes in cognitive and affective domains. Information of WISC-R contains items of structuring thinking, disordered in patients with brain damage; most tests are time limited, which reduces patients outcomes. CONCLUSIONS: Reliable assessment of neuropsychological functioning in brain tumors survivors requires a specialized evaluation process. This new tool is designed for screening, diagnosis, prognosis and treatment. Our tool is designed specifically for brain tumor survivors and should be recommended for diagnosis of specific neuropsychological consequences.

NP-006. NEW APPROACH TO ASSESSMENT OF NEUROPSYCHOLOGICAL LATE EFFECTS IN CHILDHOOD BRAIN TUMOR SURVIVORS. CHALLENGES AND BENEFITS OF THE NEW METHODOLOGY

Joanna Kornienczewska, Bozena Debtowska-Baginska, and Marta Perk-Polnick; The Children’s Memorial Health Institute, Pediatric Oncology Department, Warsaw, Poland

PURPOSE: The purpose of the study was to analyze the usefulness of standard psychological and neuropsychological assessment tools used in evaluating neuropsychological consequences of childhood brain tumors. The hypothesis was that in this specific group of patients standard tests are not sufficient to evaluate long effects of childhood brain tumors.

METHOD: The base of the study was psychological repeated testing performed in 350 childhood brain tumor survivors (various tumors types and localizations). Age at psychological diagnosis: 6 to 26 years. Full psychological outcome included assessment of problems with: memory, visual-motor skills, attention, flexibility, problem solving, semantic memory and fluency, processing speed. The patients were examined by using standardized psychological and neuropsychological methods, mainly: Wechsler Intelligence Scales; Benton Visual Retention Test; Bender + E. Koppitz Visual Motor Test; Rey – Osterrieth Complex Figure Test; Auditory Verbal Learning Test. Meta-analysis of results to verify the accuracy, relevance and reliability of the standard tests used to assess cognitive status of these patients was performed.

RESULTS: Our results showed that the majority of childhood brain tumor survivors used psychological tests failed to detect impairments. In five out of six initially incongruent patients the neuropsychological profile was in accordance with MRI findings when evaluating all data with the multidisciplinary holistic approach. CONCLUSIONS: Cognitive outcome in survivors of paediatric brain tumours depends on many different detrimental processes and shows high individual variation. Congruity between neuropsychological impairment and MRI findings might at first seem low. However, in the perspective of a clinical holistic evaluation of MRI findings and neuropsychological outcome considering the knowledge of clinical data such as type and location of the brain tumour, type of MRI findings (atrophy, gliosis, post-operative lesion), undergone treatments and radiation field as well as premorbid cognitive impairment congruity increases.

NP-007. LONG-TERM NEUROCOGNITIVE FUNCTIONING IN A CASE SERIES OF MEDULLOBLASTOMA SURVIVORS: THE IMPACT OF CEREBELLAR MUTISM SYNDROME

Karen Walsh, Anthony Goosa; Elizabeth Wells, and Roger Packer; Children’s National Medical Center, Washington, DC, USA

OBJECTIVE: About 25% of pediatric patients with medulloblastoma develop Cerebellar Mutism Syndrome (CMS) post-resection, and worse neurocognitive outcomes have been reported but not systematically studied beyond Global IQ. We aim to present a matched case series of children with medulloblastoma with and without CMS on a range of neuropsychological functions. We predict that CMS+ children will perform worse than CMS- children and will have a greater prevalence of clinical impairments. PARTICIPANTS AND METHODS: We present 5 matched pairs of medulloblastoma patients off-treatment for at least 1 year; half were CMS+. Participants were matched by diagnosis age, age at assessment, and treatment. All participants underwent a full neuropsychological evaluation. Descriptive data was calculated, and variables were dichotomized for clinical significance at one standard deviation below the mean.

RESULTS: Age range was 11-18 yrs at time of evaluation (M = 14.6; SD = 2.41), with 50% males. Time off treatment for the CMS+ participants ranged from 1-13 yrs (M = 7.0; SD = 4.18), and 1-8 yrs (M = 4.0; SD = 2.34) in the CMS- group. 90% received radiation. CMS+ participants consistently showed scores below CMS- on Performance IQ, particularly Matrix Reasoning. PIQ was impaired in 80% of the CMS+ group and never in the CMS- group. Verbal IQ was impaired in 40% of the CMS+ group, and none of the CMS-. Similar patterns emerged for working memory, flexibility, memory, processing speed, and visual-motor integration. CONCLUSION: Based on this matched sample of medulloblastoma survivors, results suggest that CMS is associated with greater impairments across a range of neurocognitive functions (not just language) in the years following treatment. This lends support to the idea that the presence of CMS is an indication of a disruption in cortical pathways associated with higher-order cognitive development and functioning.

NP-008. EPISODIC MEMORY IMPAIRMENTS IN PEDIATRIC TEMPORAL BRAIN TUMOR PATIENTS

Christelle Doger de Spéville1, Christelle Dufour2, Stéphanie Bollé3, Kim Giraudat4, Audrey Longaud5, Virginie Kieffer3, Jaques Grill3, Stéphanie Puget4, Dominique Valteau-Couzan1, Lucie Hertz-Pannier1, and Marion Nouhiane2; 1U1169, INSERM - CEA/NeuroSpin/UNIAC; Université Paris Descartes- Département de Cancérologie de l’enfant et de l’adolescent, Institut Gustave Roussy, Paris, France; 2U1169, INSERM - CEA/NeuroSpin/UNIAC- Université Paris Descartes, Paris, France; 4Département de Cancérologie de l’enfant et de l’adolescent, Institut Gustave Roussy, Université Paris Sud, Villejuif, France; 5Service de Neurochirurgie Pédiatrique- APHP Necker-Enfants Malades, Université Paris Descartes, Paris, France

BACKGROUND: Memory impairment has been reported in paediatric brain tumor patients using global neuropsychological assessments, but no study focused on long-term memory consolidation processes have been conducted in these children. Therefore, we tested a long-term memory retrieval paradigm in children treated for temporal brain tumors. METHODS: We included 10 patients (6 to 18 yrs) treated for a malignant (N = 6) or benign (N = 4) temporal brain tumor in the Paediatric Department of Gustave Roussy Institute (France) and 12 matched controls (6 to 18 yrs.). The protocol involved two parts: 1) 9 recent daily memories were first collected, 2) after a delay of 16 days, a free recall (FR) of memories was requested. When memories were not retrieved in FR, a semantic cues recall (CSR) was performed. We first analyzed the accuracy of memory retrieval (QM) in part 2 and then, the qualities of memories using the episodic

Abstracts
NP-009. PREOPERATIVE NEUROPSYCHOLOGICAL AND BEHAVIORAL EVALUATION OF CHILDREN WITH THALAMIC TUMORS

Daniela Cheffig, Giampiero Tamburini, Massimo Caidarelli, and Concezio Di Rocco; Child Neurology and Psychiatry Catholic University of Sacred Heart, Rome, Italy

INTRODUCTION: Functional involvement of the thalamus in cognitive processing has been only anecdotally reported in the literature and mostly related to thalamic haemorrhages; there is no available information on cognitive development in children with thalamic tumors. CLINICAL MATERIALS AND METHODS: All the children admitted with a diagnosis of thalamic tumor at our Institution between January 2008 and January 2011 were considered for the present study. Exclusion criteria were: age under 18 months and the presence of severe neurological deficits, both preventing a reliable neuropsychological evaluation. A complete preoperative neuropsychological evaluation was performed. RESULTS: Twenty children were selected (mean age 102.4 months). Total IQ was in the normal range in all patients (mean: 90.1; SD: 13.87) with a significant difference between VIQ (mean 97, 70 SD 17.77) and PIQ (84.82 SD 17.01). A significant correlation was found between global IQ and histological finding of low grade tumors (p = 0.001). Children with mesial thalamic tumor had higher working memory deficit and delayed recall disorders (p = 0.001). Naming disorders were related to the presence of a bilateral apical (p = 0.000) atrophic thalamic tumor (p = 0.001) without a significant difference between the involvement of the left or right hemisphere. A significant correlation was also found between the presence of neurolinguistic disorders and mesialy located tumors (p = 0.01). Children with right sided tumors had more frequently constructional praxia and executive function disorders (p = 0.0005). CONCLUSION: The present study suggests that differently located thalamic tumors might have specific neuropsychological profiles.

NP-010. NEUROCOGNITIVE DEFICITS IN CHILDREN WITH BRAIN TUMOR AT DIAGNOSIS

Katja Margelisch, Martina Studer, Maja Steinlin, Kurt Leibundgut; 1Department of Pediatric Neurology, University Children’s Hospital, Berne, Switzerland; 2Department of Pediatric Hematology and Oncology, University Children’s Hospital, Berne, Switzerland; 3Center for Cognition, Learning and Memory (CCLM), Berne, Switzerland

Survivors of brain tumors are faced with a high risk for a wide range of cognitive problems and learning difficulties. These problems are caused by the lesion itself and its surgical removal as well as by the treatments to follow (chemo- and/or radiation therapy). A few recent studies have indicated that children with brain tumors (BT) might exhibit cognitive problems already at diagnosis, i.e. before the start of any medical treatment. The aim of the present study was to investigate the “baseline” neuropsychological profile in children with BT in comparison to children with an oncological diagnosis not involving the central nervous system (CNS). 20 children with BT and 27 children with an oncological disease without involvement of the CNS (age range: 6.1 to 16.9 years) were evaluated with an extensive battery of neuropsychological tests tailored to the patient’s age. Furthermore, the child and its parents completed self-report questionnaires about emotional functioning and quality of life. In both groups, tests were administered in the areas of perception, reasoning, processing speed, language, learning and memory (CCLM), Berne, Switzerland.

For ecological neuropsychological tests, the BADS-C (Behavioral Assessment of the Dysexecutive Syndrome for Children) an ecological battery and the BRIEF questionnaire were performed for parents and teachers of child or adolescent, both for children and adolescents treated for benign and malignant frontal lobe tumors. To measure and to evaluate executive functioning in our population, both ecological valid tests and a classical evaluation of executive functions was performed. For ecological neuropsychological tests, the BADS-C (Behavioral Assessment of the Dysexecutive Syndrome for Children) an ecological battery and the BRIEF questionnaire were performed for parents and teachers of child or adolescent, both for children and adolescents treated for benign and malignant frontal lobe tumors. To measure and to evaluate executive functioning in our population, both ecological valid tests and a classical evaluation of executive functions was performed. The second aim of the study was to assess correlations between the classical tests and ecological tests, such as the BADS-C and the BRIEF questionnaire in our population. The third aim of the study was to identify and to determine factors (medical factors, social factors) influencing performance in our population. METHOD: Between September 2010 and June 2012, 21 patients treated for frontal benign/malignant lobe tumour were included aged 8-21 years at time of evaluation. Age at surgery was 8.3 years old. A comparison group of 42 patients were matched on gender, age and level education, on classical tests and on the BADS-C battery.

RESULTS: Statistical analysis of our study revealed executive functions disturbances in children and adolescents. Working memory disabilities, planning and organisation was found in both classical and ecological tests in our population. Significant and strong correlations were found between IQ measures and EF measures. Medical factors were identified on performances based in our population, such as epilepsy in our population, for medical factors, and socioeconomic status for social factors.
CONCLUSIONS: Findings suggest both PT and XRT are associated with cognitive risk. While the rate of IQ decline did not differ significantly between RT types in this sample, IQ scores in the XRT group started and remained lower compared to the PT group, possibly differences in neurocognitive toxicities between RT types should be considered. Replication with a larger sample and examination of longer-term cognitive outcomes, particularly for non-CGI PT patients, are needed.

NP-013. NEUROCOGNITIVE SCREENING TOOL FOR PEDIATRIC BRAIN TUMOR: RELIABILITY AND VALIDITY
Betty Herrington, Joseph Raiker, Edward Manning, Janie Criddle, and Cynthia Karlson; University of Mississippi, Jackson, MS, USA

PURPOSE: Research on pediatric brain tumor (PBT) patients has identified long-term neurocognitive deficits in attention, memory, and executive functioning. There is a need for brief neurocognitive screening measures that can readily detect impairment and be easily administered to guide early intervention. This study examined the reliability and validity of the Lebby-Asbell Neurocognitive Screening Examination (LANSE) for PBT patients in a clinical setting. METHODS: Participants were 53 PBT patients (M age = 10.90, SD = 3.26; 52.8% White; Med months from diagnosis = 93.00, SD = 46.24) and 30 comparison traumatic brain injury (TBI) patients (M age = 11.89, SD = 4.08; 50% Caucasian; Med months from injury = 133.00, SD = 61.19). The LANSE is a brief (20-25 minutes) measure of patient orientation, attention, executive functioning, language, verbal and visual memory, and visual-spatial functioning normed on children with TBI. BT and TBI patients between the ages of 6 to 17 years were administered the LANSE by trained psychology staff. A subset of children with PBT and TBI (n = 6 to 18) also completed the Wechsler Intelligence Scale for Children (WISC-IV, CVLT-C), and Lebby-Asbell Neurocognitive Screening Test (LANSE) and Children’s Memory Scale (CMS). RESULTS: PBT patients exhibited a similar degree of impairment as TBI patients on the LANSE. Specifically, PBT patients exhibited similar impairments as TBI patients across the domains of attention, language, executive functioning, as well as visual and verbal memory. These domains showed good reliability (α’s ranged from 0.67 to 0.88) and correlated significantly in the hypothesized direction with similar domains on the WISC-IV, CVLT-C, and Lebby-Asbell Neurocognitive Screening Test (p ≤ 0.55 to 0.93). CONCLUSION: Screening results from the LANSE are consistent with full neurocognitive examination results reported in the literature. The LANSE is a reliable and valid screening measure easily administered in clinic that may be a valuable tool for detecting neurocognitive impairment during and after treatment.

NP-014. NEUROPSYCHOLOGICAL FOLLOW-UP OF HEAD START II SURVIVORS: AN UPDATE
Whitney Guerry, Jonathan Finlay, and Stephen Sand; 1Columbia University Medical Center, New York, NY, USA; 2University of Southern California Keck School of Medicine, Los Angeles, CA, USA

PURPOSE: Given the neuropsychological deficits associated with irradiation in young children diagnosed with malignant CNS tumors, the Head Start II protocol employed high-dose myeloablative chemotherapy followed by autologous hematopoietic cell transplantation to avoid or delay clinically-irradiated irradiation. This research examined long-term neuropsychological functioning of patients treated on the Head Start II protocol between 1997 and 2003. METHODS: Patients completed baseline testing prior to autologous transplantation and biannually thereafter. Assessments were completed for 49/51 (96%) patients at baseline (T1 mean age = 3.4 years; SD = 2), Twenty patients passed away between T1 and T2. 27/31 (87%) completed assessments at T2. 16/31 (52%) at T3, 6/31 (19%) at T4, and one at T5. Analyses compare neuropsychological functioning at baseline to most recent follow up assessment (T2 to T5; mean length of follow up = 7.39 years, SD = 3.21) and examine outcomes for patients who received intravenous methotrexate (MTX), and visual-spatial functioning compared to those who did not. RESULTS: Independent samples t-tests comparing performance at baseline and most recent follow-up revealed no significant change over time on FSIQ, PIQ, VIQ, reading, spelling, math, general memory, verbal or visual delayed memory, for the entire group. Full Scale IQ change over time was expected to decrease by 0.43 points). Although not significant, PIQ scores declined 3.25 points and VIQ scores increased 3.25 points from baseline. Mean scores at most recent follow-up indicate that survivors performed worse than their age-matched peers (all p < 0.001). The most recent treatment group means did not reveal any significant differences; with the exception of lowered visual delayed memory for those who received IVMTX (p = 0.03). CONCLUSIONS: These analyses include neuropsychological outcome data for children up to 12 years post-diagnosis of a malignant CNS tumor, indicating that children treated with a protocol aimed to reduce late effects on neurocognitive development continue to display broadly stable neuropsychological functioning over extended follow-up.

NP-015. WHITE MATTER DAMAGE DISRUPTS NEURAL PHASE SYNCHRONY AND IMPAIRS COGNITIVE PERFORMANCE IN CHILDREN TREATED WITH CRANIAL RADIATION FOR BRAIN TUMOURS OF THE POSTERIOR FOSSA
Colleen Dockstader, Jovanka Skocic, Eric Bouffet, Suzanne Laughlin, Uri Tabori, and Donald Mabbot; The Hospital for Sick Children, Toronto, ON, Canada

Cognitive impairments are consistently reported in children treated with cranial radiation (CRT) for brain tumours. These deficits are, at least in part, related to white matter damage. We investigated how white matter damage and poor task performance related to neural function by comparing functional measures obtained with Magnetoencephalography and structural measures obtained with Diffusion Tensor Imaging to visualize-motor task performance in eighteen healthy children (12M/6F; 11.3 yrs +/− 3.5) and 20 pediatric Posterior Fossa (PF) brain tumour patients (13M/ 7F; 12.07 yrs +/- 2.58) who had been treated with CRT (15 medulloblastoma, 3 ependymoma, all received CRT treatment of either focal [PF only] or whole-brain boost, chemotherapy (all patients) and PF boost). White matter health/injury measures predicted reaction times in both groups. White matter structure predicted faster reaction times on task performance in both healthy children (r = −.72, p < .001) and patients (r = −.52, p < .05). Functionally, phase synchrony of the visual cortex in response to the visual cue was the best predictor of performance. Phase synchrony is the temporal consistency of the neural response from trial to trial and reflects the coordination of neural communication across brain structures. In healthy children, phase synchrony was correlated with increased white matter health (r = .64, p < .01) and faster reaction times (r = −.51, p < .05). In patients, decreased phase synchrony was correlated with decreased white matter health (r = −.35, p < .05) with no relationship to reaction time. We propose that the condition of white matter influences reaction time on a visual-motor task through the temporal coordination of information arriving at the visual cortex. The phase synchrony of the neural response may be a biomarker of white matter injury and cognitive impairment in children treated for brain tumours.

NP-016. LONG-TERM OUTCOME IN SUBGROUPS OF MEDULLOBLASTOMA
Iska Moreen-Emre1, Nadia Scantlebury1, Michael D. Taylor1, Eric Bouffet2, David Malkin3, Suzanne Laughlin4, Nicole Law5, Toshihiro Kunimae6, Jeffery Leonard7, Josh Rubin8, Shin Jung9, Seung-Ki Kim10, Nalin Gupta11, William Weese12, Claudia Farra13, Rajeev Vihbar13, Brenda Spiegel13, Laura Janzen13, Fang Liu13, Lexi Decker13, and Donald Mabbot14; 1The Hospital for Sick Children, Toronto, ON, Canada; 2Tohoku University Graduate School of Medicine, Sendai, Japan; 3St. Louis Children’s Hospital, St. Louis, MO, USA; 4Chonnam National University, Channom, Republic of Korea; 5Seoul National University Children’s Hospital, Seoul, Republic of Korea; 6University of California San Francisco, San Francisco, CA, USA; 7Hospital de Santa Maria, Lisbon, Portugal; 8University of Colorado Denver, Aurora, CO, USA

BACKGROUND: Treatment for medulloblastoma is associated with white matter damage and cognitive morbidity. Reducing treatment in subgroups of medulloblastoma with better prognosis could spare certain group(s) from neuro-toxic complications. We examined relations between subgroup (WNT, SHH, Group 3, Group 4) and late effects to identify differences in long-term outcome. METHODS AND RESULTS: (i) Quality-of-life data (Health Utilities Index) were collected from 67 patients (6 WNT, 18 SHH, 11 Group 3, 27 Group 4, 4 unclassified) across 8 sites in the Medulloblastoma Advanced Genomic International Consortium. Of 13 attributes assessed, only cognition differed between subgroups; the mean single-attribute utility score was higher for SHH (0.98 ± 0.03) than Groups 3 (0.95 ± 0.04; p = 0.007) and 4 (0.96 ± 0.03; p = 0.029). We further investigated cognitive outcome by comparing rate of change in (ii) intellectual functioning of 91 patients (41 Group 4; 20 Group 3; 18 SHH; 12 WNT) treated at SickKids. WNT was excluded from the following analyses due to its relatively small sample size. Groups 3 and 4 declined by ~4.5 IQ points/year (p ≤ 0.001) and visual delayed memory (p = 0.18). A subset of these patients (14 Group 4; 6 Group 3; 8 SHH) and 38 controls underwent diffusion tensor imaging to assess (iii) white matter microstructure and identify potential structural correlates of cognitive morbidity. Relative to controls, Group 3 had reduced MD/MFA (+0.03 ± 0.009; RD = 0.000041 +
NP-017. PREDICTORS OF INTELLIGENT FUNCTIONING IN NEWLY DIAGNOSED CHILDREN WITH A BRAIN TUMOR
Jurgen Lemiere1, Todd Vercruysse1, Monique Haers1, Jurgen Lemiere2, Trui Vercruysse2, Monique Haers2, Sam Geuns3, Sandra Jacobs3, and Stefaan Van Gool3; University Hospitals KU Leuven, Paediatric Haematology-Oncology, Leuven, Belgium

Children diagnosed and treated for a brain tumor often experience cognitive problems. Identification of factors associated with the tumor and its treatment having an impact on cognitive functioning is relevant. However, most studies investigating these factors are retrospective, making it difficult to disentangle the effects of the tumor, the acute (e.g., hydrocephalus) and treatment (e.g., radiotherapy) phase. The aim of the present study is to investigate intellectual functioning after a diagnosis of a brain tumor and to identify predictive factors for intelligent functioning in these children. A total of 68 children diagnosed with a brain tumor at the UZLeuven between 1996 and 2013 enrolled the study and were tested with the age-appropriate Wechsler scale. This was conducted as soon as possible after diagnosis and before initiation of further treatment with chemo- or radiotherapy. Neuropsychological testing was conducted 10.2 (SEM = 2.47) times per week for 3 months. Participants were evaluated at baseline (T1) and post-intervention (T2). The TXT group participated in a group exercise intervention program (Chakravarty et al., 2013) and volumes were corrected for scanner type and age. RESULTS: A repeated measures ANOVA revealed a significant decline in hippocampal volume in the MB group (t(34) = 25.43, p < 0.001). At the 3 months follow-up, hippocampal volumes of the TXT group at T2 (1974.08 mm³) resembled those of healthy controls (1981.38 mm³) reported in our earlier study (Riggs et al., epub ahead of press). At the 3 months follow-up, hippocampal volumes of the TXT group increased significantly and remained significantly higher than volumes in the CTRL group (t(34) = 25.43, p < 0.001). Multiple regression analyses demonstrated that the proportion of children showing ‘below average’ intellectual performance was significantly lower in the TXT group than in the CTRL group (F(1,3275.04 mm³), p = 0.008). Significant group by time interaction (F(1,14) = 3275.04 mm³, p < 0.001). Our results suggest that aerobic exercise may be an effective intervention in repairing some of the damage following radiation. Future work will examine the relation between hippocampal volume increase and cognitive change, particularly in learning and memory.

NP-019. HIPPOCAMPAL VOLUMES DECREASE OVER TIME IN CHILDREN TREATED FOR MULLLOBLASTOMA
Lily Riggs1, Eric Bouffet1, Mallar Chakravarty2, Suzanne Laughlin1, Normand Laperrere3, Fang Liu1, Jovanka Skocic1, Jinn Phippiones4, Susan Hasel2, Karen Hasel4, Christopher Boulanger1, Douglas Strother4, Juliette Hukin5, Christopher Fryer5, Dina McConnell5, Douglas Strother4, Juliette Hukin5, Christopher Fryer5, Dina McConnell5, Janet Almeida6, Jurgen Lemiere7, Trui Vercruysse7, Monique Haers2, Sam Geuns3, Sandra Jacobs3, and Stefaan Van Gool3; 1The Hospital for Sick Children, Toronto, ON, Canada; 2Centre for Addiction and Mental Health, Toronto, ON, Canada; 3University of Calgary, Calgary, AB, Canada; 4British Columbia Children’s Hospital, Vancouver, BC, Canada

OBJECTIVES: The hippocampus is critical for learning and memory. Children treated for medulloblastoma exhibit lower memory performance and smaller hippocampal volumes as compared to healthy controls (Riggs et al., epub ahead of press). However, it is not clear how hippocampal volumes change over time, and how such changes may deviate from normal development. The current study is the first to examine longitudinal changes in hippocampal volume in both a medulloblastoma (MB) and healthy control (HC) group. PARTICIPANTS AND METHODS: 16 MB (age = 9.02 ± 2.47) and 20 HC participants (age = 9.70 ± 2.21) were included. Follow-up scans were obtained annually over 4 years using a 1.5T Siemens, 1.5T GE or a 3T GE scanner. For the MB group, the first scan occurred at around the time of diagnosis (i.e. baseline). All participants had at least two scans. The hippocampus was defined using an automated segmentation program (Chakravarty et al., 2013) and volumes were corrected for intra-cranial volume, scanner type and age. RESULTS: A mix model regression model was used to examine changes in hippocampal volume over time. This revealed a significant decline in hippocampal volume in the MB group (p = 0.0021), but not in the HC group (p = 0.049). In the MB group, there was an estimated 2.89% decrease in hippocampal volume each year (baseline = 3568.14 mm³, 3 year follow-up = 3275.04 mm³). CONCLUSIONS: The current results show that treatment for MB is associated with atypical development of the hippocampus in children. Future work will examine the impact of clinical factors such as radiation dose and the occurrence of hydrocephalus on hippocampal volume and its developmental trajectory.

NP-020. PSYCHOLOGICAL ASSESSMENT IN CHILDREN WITH TUMORS OF POSTERIOR FOSSA: FROM DIAGNOSIS TO FOLLOW UP
Domitilla Elena Secco1, Simona Cappelletti, Simonetta Gentile1, Damila Cherifen1, Antonella Cacchione, Francesca Del Bufalo1, Susanna Staccioli2, Alessandra Spagnoli, Raffaella Messina1, Andrea Carai1, Carlo Eufizio Marrazza, and Angelo Mastronuzzi; Bambino Gesù Children’s Hospital, Rome, Italy

Lesions of the posterior fossa account for 20% of all the patients with brain tumors and although tumor related neuropsychological sequelae have been reported, few data describe the psychosocial consequences faced at the end of the treatment. We assessed emotional, behavioral and social impairments from diagnosis to follow-up (6-12 months), in children referred to our institution, using the Achenbach Child Behavior Checklist for ages 1-5 years (group-1) and 6-18 years (group-2). The possible correlation between impairments and tumor’s location was also evaluated. We enrolled 23 patients (14 M, 9 F): 11 (48%) in group-1 and 12 (52%) in group-2. Mean age was 89 months at diagnosis and 101 months at follow-up. The location was vermis in 8 patients (35%); emispheric in 2 (9%), vermian-emispheric in 3 (13%) and extending to the fourth ventricle in 3 (13%). Most frequent histology was medulloblastoma (74%), followed by pilocytic astrocytoma (18%) and ependymoma (8%). All the patients underwent surgical resection, 14 patients (61%) received chemotherapy, 8 (35%) chemotherapy and radiotherapy. Mean Internalizing scores were 52 at diagnosis and 53 at first follow up in group-1, 57 and 64 respectively in group-2. Mean Externalizing scores were 47 and 53 for younger children and 46 and 51 for the other group (diagnosis and follow-up, respectively). Changes of emotional, behavioral and social profiles were not found to be significant in both groups. A trend toward increase of attention issues was found in patients with less involvement of the fourth ventricle. Our preliminary data

NEURO-Oncology • June 2014 i103
suggest that emotional, behavioral or social impairments at diagnosis tend to stably persist throughout treatment and must then be target of early intervention. Moreover, specific neuropsychological rehabilitation might be beneficial in cases of lesions involving the fourth ventricle. A larger cohort of patients and longer follow-up are required to better characterize our results.

**NP-021. SOCIA9 COGNITIVE DEFICITS AND REDUCED SOCIAL ATTAINMENT IN ADULT SURVIVORS OF CENTRAL NERVOUS SYSTEM (CNS) TUMORS**

Tara Brinkman, Gregory Armstrong, Cara Kimberg, Amar Gajjar, Deo Kumar Srivastava, Leslie Robison, Melissa Hudson, and Kevin Krull;
St. Jude Children’s Research Hospital, Memphis, TN, USA

**BACKGROUND:** Pediatric CNS tumor survivors are at risk for neurocognitive impairment, yet little is known about social cognition in adult survivors. **METHODS:** Participants included 78 adult survivors of childhood CNS tumors (53% infratentorial, 45% supratentorial) enrolled in the St. Jude Lifetime Cohort (mean SD current age = 28.1 years [5.8], at diagnosis = 9.4 years [4.7], and time since diagnosis = 18.8 years [6.0]). Age-adjusted standard scores were calculated for measures of intelligence and social cognition including affect recognition (i.e. facial expression of emotion) and prosody (i.e. emotional tone of voice). Impairment was defined as performance > 1 SD below the normative mean. Multivariable general linear models were used to examine associations between tumor location and treatment and social cognition. Logistic regression models examined association between social cognitive outcomes and virotherapy. **RESULTS:** 30% of CNS tumor survivors were impaired on measures of facial affect labeling (p = 0.001), 32% for identifying prosody (p < 0.001), and 34% for matching prosody with nonverbal social cues (i.e. body posture, affect; p < 0.001). Infratentorial tumor survivors treated with craniospinal radiotherapy (CSI) performed significantly worse than infratentorial tumor survivors treated with focal RT, supratentorial survivors treated with focal RT, and survivors treated with no CRT on facial affect naming (p = 0.017), prosody identification (p < 0.001), and matching prosody with social cues (p = 0.007). These differences persisted after accounting for IQ. In models adjusted for IQ, sex and age, better performance on social cognition tasks increased the likelihood of full time employment by 5% (OR = 1.5, 95% CI 1.2-2.1) and independent living by 20% (OR = 1.2, 95% CI, 1.1-1.4). **CONCLUSIONS:** Adult survivors of pediatric CNS tumors demonstrated considerable impairment on measures of social cognition, with greater impairment observed for survivors of infratentorial tumors treated with CSI. Observed social impairment confers risk for reduced occupational attainment in adulthood and may have implications for the social independence and achievement of survivors.

**NP-022. COMPUTERIZED ASSESSMENT OF NEUROCOGNITIVE FUNCTION IN PRESCHOOL- AND SCHOOL-AGED CHILDREN WITH BRAIN TUMORS**

Kristina Hardy, Sarah Hostetter, Eugene Hwang, and Karin Walsh;
Children’s National Health System, Washington, DC, USA

**OBJECTIVE:** Psychometrically-valid and reliable neurocognitive assessment tools for young children are lacking, particularly for domains affected by brain tumors and their treatment. We examined the utility and construct validity of a brief, computerized assessment in a sample of preschoolers (aged 4-6) and school-aged children (aged 7-16) diagnosed with brain tumors (BT).

**METHODS:** Five computerized tasks using touch-screen technology were developed using theCogState assessment platform. Two versions of the tasks were used: one tailored for children 4-6 and one developed for older children and adolescents. Tasks included measures of processing speed, visual attention, working memory, visual learning, and executive functioning. Children completed these tasks as well as traditional measures of intellectual, memory, visual-motor, and executive functioning. **RESULTS:** To date, 37 children with BT (M age = 10.4, 60% male, 84% White) have completed computerized testing. Participants ranged from 0-14 years since diagnosis (M = 4.5 years), 50% had received cranial radiation therapy. Mean intellectual functioning and parent-rated working memory were in the average range (FSIQ = 99.4, SD = 18.93), BRIEF Working Memory T = 57.9, SD = 12.99; CBCL/BASC Attention T = 52.4, SD = 8.30). Data supported the convergent validity of many computerized tests for both the preschoolers and school-aged groups. For example, worse performance on a computerized Stroop task was associated with executive dysfunction (r = 0.41, p < 0.05), longer time since diagnosis (r = 0.35, p < 0.05), and younger age at diagnosis (r = -0.43, p < 0.05).

**CONCLUSIONS:** Computerized cognitive testing has potential advantages over traditional paper-and-pencil measures for children with BT at risk for neurocognitive sequelae, including brevity, multiple alternate forms, and reduced motor demands. If reliable and valid, these tasks could serve as rapid, low-cost cognitive monitoring tools that can be administered within an on-site neuropsychologist.

**NP-023. NEUROINFO FOR KIDS – DEVELOPMENT OF A MANUAL TO HELP CHILDREN WITH A BRAIN TUMOR TO MAKE THE BEST OUT OF THEIR NEUROPSYCHOLOGICAL TEST RESULTS**

Ulrike Leiss1, Anna Bemmer2, Thomas Pletschko1, Juergen Grafeneder1, Agathe Schwarzinger2, Pia Deimann2, and Irene Slave1;
1Department of Pediatrics, Medical University of Vienna, Vienna, Austria; 2Faculty of Psychology, University of Vienna, Vienna, Austria

As survival rates in pediatric neuro-oncology have risen over the past decades, tumor- and treatment related neuropsychological late effects remain problematic for survivors. Various guidelines emphasize the importance of neuropsychological evaluation at different time points and give recommendations concerning the way assessment is carried out. However, the test situation itself as well as the report of the test results can be very challenging for the survivors, possibly facing their own deficits and therefore feeling degraded. For this reason we developed a standardized, resource-oriented manual facilitating the reporting of test results, NeuroInfo for Kids (NIK). NIK is based on the concept of salutogenesis and focuses on empowering the child, and/or his/her caregiver, through helping the child to get realistic knowledge of his own strengths and weaknesses and to get ideas of how to best deal with potential deficits. PARTICIPANTS: 23 patients with different types of brain tumors at the Department of Pediatrics, Medical University of Vienna; 12 girls, 11 boys; mean age 10.7 [7-13] years; mean age at onset 5, 61; mean time since onset 5,39; treatment with surgery, chemotherapy and/or radiotherapy. METHODS: The first draft of NIK was evaluated in a pilot study, with respect to the study questions whether NIK has an influence on comprehensibility, manageability and the feeling of meaningfulness. The young patients had to fill out standardized questionnaires before and after the intervention with NIK, which was carried out by a trained neuropsychologist. SPSS was used for statistical analysis. RESULTS: We found that NIK significantly increased knowledge about personal strengths and weaknesses. Moreover knowledge about possible interventions was significantly improved. However, general knowledge about neuropsychological assessment could not be increased. Besides, NIK had no impact on self-esteem of the participants. As a result of the pilot study the improved version NIK was defined.

**NP-024. COGNITIVE OUTCOMES IN MEDULLOBLASTOMA PATIENTS WITH CEREBELLAR MUTISM AND SHUNTED HYDROCEPHALUS**

Patti Batchelder1, Greta Wilkening1, Todd Hankinson1, Nicholas Foreman1, and Michael Handler2; 1Children’s Hospital Colorado, Aurora, CO, USA; 2University of Colorado School of Medicine, Aurora, CO, USA

**PURPOSE:** Medulloblastoma survivors have lower cognitive scores than healthy peers, attributed to radiation therapy. We sought to assess the impact of cerebellar mutism and shunted hydrocephalus. **METHODS:** A retrospective chart review was completed of all 95 medulloblastoma patients treated at our institution between 1981 and 2015. Patients were excluded for age older than 21 years (4), incomplete data (8), no surgical resection (2), and rapid death (1). 80 charts were reviewed for age at diagnosis, sex, treatment, diagnosis of cerebellar mutism, presence of cerebral spinal fluid (CSF) shunt, and results and timing of cognitive testing. RESULTS: Of 38/80 had documented post-treatment neuropsychological evaluations, 26 males and 12 females, with a mean age of 6.2 years at diagnosis. 37/38 received radiation. 10 had cerebellar mutism, 8 a CSF shunt, and 4 had both. All (M age = 10.4; 60% male, 84% White) had cognitive mean of 100. In those with a CSF shunt it was 87, and 71.7 in those with cerebellar mutism. Performance was weakest in patients with cerebellar mutism and a CSF shunt, 67. Verbal scores were better than Perceptual and Working Memory measures in all groups. Processing speed was low to below average in all. CONCLUSION: With parent engagement in all, CONCEPTS: After treatment of medulloblastoma, patients demonstrate lower than average cognitive scores. Cerebellar mutism worsens the outcome further, particularly in patients requiring a shunt.