RARE-07. Low resting energy expenditure is associated with clinical and radiological hypothalamic damage in children surviving a suprasellar brain tumor

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etic neurodevelopmental syndromes such as Prader-Willi syndrome and septo-optic dysplasia. Hypothalamic syndrome is characterized by intractable weight gain associated with severe morbid obesity and memory impairment, attention deficit, reduced impulse control as well as increased risk of cardiovascular and metabolic disorders. Currently, there is no cure for this condition. Treatments used for general obesity such as surgery, medication and counselling are often tried in hypothalamic syndrome, but are mostly ineffective, and there are no medications specifically approved for hypothalamic syndrome. The most important aspects of presentation and outcome of hypothalamic syndrome due to different neuro oncological diseases, its risk factors and an overview of currently available therapeutic interventions aiming to decrease and ameliorate the consequences of hypothalamic dysfunction will be presented. Furthermore, novel aspects and perspectives for future research will be discussed.

RARE-05. LEGAL DEGREE OF DISABILITY IN CHILDHOOD-CRANIOPHARYNGIOMA SURVIVORS DURING LONG-TERM FOLLOW-UP – RESULTS OF THE HIT-ENDO STUDY

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BACKGROUND: Craniopharyngiomas are rare low-grade embryonic malformational tumors of the sellar/parasellar region. The prognosis after diagnosis during childhood and adolescence is influenced by endocrine and hypothalamic long-term sequelae. A legal status of the degree of disability (GdB), according to the German Social Code Book V that is worthy of support, provides financial means for psychosocial rehabilitation and participation of craniopharyngioma survivors. The aim of this study was to determine the association of clinical/psychosocial characteristics and quality of life (QoL) indicators with the resulting GdB. PATIENTS AND METHODS: HIT-Endo is a German registry study on craniopharyngioma patients aged ≤ 18 years at diagnosis and included before the year 2000. In a sample of 108 patients, the degree of disability and the association with endocrine, ophthalmological, neuropsychological and psychosocial parameters was analyzed after a mean follow-up period of 16 years (95% CI: 9.8-36.4). RESULTS: 44 patients (41%) did not receive a GdB, three patients (3%) received a GdB of 30-40, 43 patients (40%) a GdB of 50-90 and 18 patients (17%) the maximum GdB of 100. Higher GdB were associated with lower education, higher body mass index standard deviation and a higher degree of visual impairment and hypothalamic involvement of the craniopharyngeoma. Patients with a GdB of 100 reported loss in physical and cognitive function, as well as fatigue, dyspnea, and pain conditions, and limitations in social and occupational contexts. They further had a lower functional capacity (German daily life ability scale (FMH)) compared to those with a smaller GdB. CONCLUSION: The GdB is associated with psychosocial and physical impairments and reflects the long-term consequences of craniopharyngioma during childhood and adolescence. A low functional capacity (assessed by FMH) may indicate the eligibility for a high GdB in later life of craniopharyngioma survivors.

RARE-06. EXPANDING THE CLINICAL AND MOLECULAR SPECTRUM OF PITUITARY BLASTOMA

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Pituitary blastomas (PitB) are rare *DICER1*-associated tumors that occur exclusively in children < 2 years of age. They are locally aggressive tumors that are driven by a combination of germline and somatic alterations involving *DICER1*. Here, we report two patients with pituitary neoplasms that expand the clinical and molecular spectrum of PitB. Patient 1 presented at 10 months with diabetes insipidus and was initially diagnosed with pituitary ependymoblastoma. She received debulking, chemotherapy and focal radiation with complete response achieved, but unfortunately died at the age of 8 years due to cerebral edema. Patient 2 was a survivor of infant leukemia who was treated with chemotherapy and then further chemotherapy with cranial irradiation at relapse. The patient was then diagnosed at the age of 8 years with pituitary CNS-PNET, which was treated with craniospinal irradiation and chemotherapy, and had remained in remission for 6 years. Review of histology in both cases indicates presence of neuroendocrine lobules, primitive cells, and Rathke pouch-like glandular structures, with high Ki67, ACTH and PRAME positivity compatible with PitB. Next-generation sequencing revealed presence of two *DICER1* mutations (germline frameshifting and somatic missense) in Patient 1, and one somatic missense *DICER1* mutation plus loss of heterozygosity in Patient 2 (no germline alteration). Surprisingly, C19MC amplification was also detected in Patient 1. Methylation profiling confirms clustering among our samples and PitB references, but not ETMR references. MicroRNA array revealed decrease in mature microRNA expression and preferential down-regulation of 5p/3p species in tumor compared to control pituitary tissue. In all, PitBs may present with clinical and molecular characteristics not conforming with the classical descriptions. It might be prudent to consider sequencing for *DICER1* alteration in pediatric pituitary tumors to facilitate diagnosis of this increasingly heterogeneous rare entity.

RARE-07. LOW RESTING ENERGY EXPENDITURE IS ASSOCIATED WITH CLINICAL AND RADIOLOGICAL HYPOTHALAMIC DAMAGE IN CHILDREN SURVIVING A SUPRASELLAR BRAIN TUMOR

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INTRODUCTION: Children with suprasellar brain damage are at risk for hypothalamic dysfunction (HD). HD may lead to decreased resting energy expenditure (REE) contributing to the development of hypothalamic obesity. Decreased REE, however, is not present in all children with hypothalamic damage. Our aim was to assess which children suspect for HD have low REE, and if REE outcome can be associated with clinical severity of HD or with radiological posterior hypothalamic damage. METHODS: A retrospective cohort study was performed evaluating all children diagnosed with brain injury at risk for HD in whom REE measurement was performed. Measured REE (mREE) was compared to predicted REE (pREE) using amongst others the Schofield equation. Low REE was defined as mREE<90% compared to pREE. Radiologic hypothalamic damage was scored using Muller grading score. The mREE/pREE quotient was associated to a clinical score for HD symptoms and to radiological hypothalamic damage. RESULTS: Sixty-seven children suspected for HD (94% brain tumor diagnosis) with a mean BMI SDS of +2.3 ± 1.0 were included. Of these, 45 (67.2%) had mREE <90% compared to the pREE. Children with severe HD symptoms had a significant lower mean mREE/pREE quotient compared to children with no, mild, or moderate HD symptoms. Mean mREE/pREE quotient of children with posterior hypothalamic damage was significantly lower compared to children with no damage or with anterior damage. Tumor progression or tumor recurrence, severe clinical HD, and panhypopituitarism with DI were significant risk factors for reduced REE. CONCLUSION: Not all children suspect for HD have a low REE. Low REE is associated with clinical and radiological scores for hypothalamic damage. REE measurements in childhood brain tumor survivors may be useful to distinguish between those who may benefit from obesity treatment that increases REE from those who would be better helped using other obesity interventions.

RARE-08. PROFILING OF RECURRENT ADAMANTINOMATOUS CRANIONPHARYNGIOMA CONFIRMS THE ACTIVATION OF THE MAPK PATHWAY AND IDENTIFIES COPY NUMBER ABERRATIONS IN RELAPSED TUMOURS

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Craniopharyngiomas are rare challenging tumours, with around 25% of cases recurring despite surgery and/or radiotherapy. Whilst transcriptomic and proteomic profiling of adamantinomatous craniopharyngioma (ACP) have revealed activation of the MAPK pathway and IL-6 mediated inflammation, relatively little is known about the biological processes involved in tumour recurrence. To address this, we have analysed a cohort of primary and relapsed ACP tumour accessed from tissue banks, local pathology departments and international collaborators. Serial samples of recurrent ACP (n=11), recurrent papillary craniopharyngioma (PCP)