Childs Nerv Syst (2005) 21: 539–545
DOI 10.1007/s00381-005-1166-9

INVITED PAPER

Hermann L. Müller
Ursel Gebhardt
Andreas Faldum
Angela Emser
Nicole Etavard-Gorris
Reinhard Kolb
Niels Sörensen

Functional capacity and body mass index in patients with sellar masses—cross-sectional study on 403 patients diagnosed during childhood and adolescence

Received: 19 January 2005
Published online: 12 May 2005

H. L. Müller (✉) · U. Gebhardt · N. Etavard-Gorris · R. Kolb
Department of Paediatrics, Zentrum für Kinder- und Jugendmedizin, Klinikum Oldenburg gGmbH, Dr.-Eden-Strasse 10, 26133 Oldenburg, Germany
e-mail: mueller.hermann@klinikum-oldenburg.de
Tel.: +49-441-4032013
Fax: +49-441-4032887

A. Faldum · A. Emser
Institute for Medical Biostatistics, Epidemiology and Informatics (IMBEI), University of Mainz, Mainz, Germany

N. Sörensen
Department of Paediatric Neurosurgery, University Hospital, Würzburg, Germany

Abstract *Rationale:* We analyzed the impact of tumour localization and histology on functional capacity (FC) and body mass index (BMI) in children with sellar masses. *Methods:* FC was evaluated using the ability scale Fertigkeitenskala Münster–Heidelberg in 403 children and adolescents with sellar masses (276 craniopharyngioma, 14 germinoma, 21 optic/chiasmatic glioma, 40 hypothalamic glioma, 13 cysts of Rathke's cleft and 39 other sellar masses). Besides tumour localization, the influence of gender, irradiation and age at diagnosis and at evaluation on FC and BMI was analyzed. General linear models with explanatory influential variables were built. *Results:* In multivariate analysis, only age at diagnosis (p<0.001) and hypothalamic involvement (p=0.005) had relevant impact on FC. The second model showed BMI at diagnosis (p<0,001), hypothalamic involvement (p<0.001) and craniopharyngioma (p=0,004) to influence BMI at the latest evaluation. *Conclusion:* We conclude that hypothalamic involvement and young age at diagnosis had major impact on FC and BMI and should be considered as risk factors for impaired rehabilitation.

Keywords Functional capacity · Sellar mass · Brain tumour · Hypothalamus · Obesity · Quality of life · Craniopharyngioma

Introduction

Craniopharyngiomas are embryogenic malformations which arise from ectoblastic remnants of Rathke's pouch. Thus, craniopharyngiomas can be found anywhere along the path of development of Rathke's pouch in hypothalamic and pituitary regions, which are of importance in endocrine regulation and satiety modulation [1]. Craniopharyngiomas are the most common intracranial tumours of non-glial origin in the paediatric population. They constitute between 1.2 and 4.4% of all brain tumours in children [2]. The peak incidence is at age 5–10 years, but they can occur at any age including infancy and prenatal and neonatal periods [3]. Although the tumour itself is benign, and the overall survival rate of patients is high [4], there is considerable morbidity even if the tumour can be resected completely [5]. In spite of sufficient substitution of hormonal deficits, obesity is present postoperatively in up to 52% of patients, with at least one half of these patients having severe difficulty controlling their desire to eat [6].

The relationship between obesity and hypothalamic damage has been extensively documented in animals. Although there have been relatively few opportunities for the systematic study of hypothalamic lesions in man, it is widely believed that the hyperphagia and obesity in craniopharyngioma are related to hypothalamic damage caused by

treatment or the tumour itself. Studies on magnetic resonance imaging (MRI) findings in childhood craniopharyngioma demonstrated a significant relation between postoperative obesity and the degree of hypothalamic damage on MRI [7]. Recent studies on body composition, functional capacity (FC) and quality of life (QoL) in patients with childhood craniopharyngioma support the hypothesis that obesity is associated with impaired FC in affected patients [4, 8, 9].

Alterations in body composition, as is the case with obesity in craniopharyngioma or cachexia in diencephalic syndrome due to hypothalamic glioma, frequently affect FC in patients with tumours of the sellar and suprasellar regions. The specific influence of tumour histology and tumour localization on prognosis and outcome in patients with sellar or suprasellar masses had not yet been analyzed in comparative studies. The aim of our study was to assess the special impact of tumour localization and histology on the rate of severe obesity and FC in childhood patients with sellar masses diagnosed during childhood or adolescence.

Materials and methods

The study was approved by the local standing committee on ethical practice, and written parental and/or patient consent was obtained in all cases.

Four hundred and three children and adolescents (208 male/195 female) with sellar and/or parasellar tumours or malformations were included in the study [276 craniopharyngioma, 14 germinoma, 21 optic/chiasmatic glioma, 40 hypothalamic glioma, 13 cysts of Rathke's pouch and 39 other sellar masses (four pituitary adenoma; three prolactinoma; four hypothalamic hamartoma; 15 suprasellar arachnoidal cyst; five central nervous system Langerhans cell histiocytosis {CNS LCH}; four sarcoma of the basal skull; four pituitary malformations)]. Patients were recruited in a study on childhood craniopharyngioma [10]. Diagnosis was made at a median age of 8.5 years ranging from 17 days to 18.0 years. Two hundred and fifty-three patients could be evaluated for weight development at a median age of 14.0 years, ranging from 0.3 to 38.7 years after a median follow-up period of 5.0 years (range, 0.1–33.7 years). FC could be evaluated in 246 patients at a median age of 13.4 years (range, 0.7–38.8 years) after a median follow-up of 4.3 years (range, 0.1–33.8 years). Tumour diagnosis was confirmed by histology or typical findings on MRI and/or computed tomography (CT). Hypothalamic involvement was evaluated based on surgical records and imaging. Tumour localization was categorized as sellar, suprasellar or sellar and suprasellar based on MRI and/or CT.

Body height was measured using a stadiometer. Body weight was evaluated by calculating the body mass index [BMI=weight (kg)/height^2 (m^2)] and expressing the BMI as a standard deviation score (SDS) using the references of Rolland-Cachera et al. [11]. BMI SDS were evaluated at the time of diagnosis and at the time of latest visit.

The ability scale Fertigkeitenskala Münster–Heidelberg (FMH) was used for self-assessment of FC [12] in patients with tumours of the sellar region. The FMH measures the capability for daily life actions with 56 items. It was standardized using 971 persons (45.5% female), with ages between 0 and 102 years, resulting in age-dependent percentiles. The retest-reliability coefficient is 0.99. The average time for answering the FMH questionnaire was 4.5 min in first-time users [13]. The questionnaire is published in a German language version. All patients were native German speakers. The questionnaire was sent out to 403 patients with masses of the sellar region. Two hundred and forty-six questionnaires returned for evaluation.

The influence of gender, irradiation, diagnosis, hypothaamic tumour involvement, tumour localization (intrasellar, suprasellar, and/or retrosellar areas), age at diagnosis, age at evaluation and time from diagnosis to evaluation on FC and BMI were analyzed.

Statistical analyses were performed using SPSS 10.0. First general linear models with explanatory influential variables were built using stepwise variable selection (inclusion/exclusion criteria, $p \leq 0.05/p \geq 0.10$, respectively) for each of the dependent variables. In a second iteration, those influential variables found to be explanatory were evaluated once again in a general linear model procedure to increase the number of valid cases. In the end, interactions between categorical explanatory influences were examined. In addition to the number of valid cases, the selected and excluded potential influences are stated for each model. Moreover, the p values of the t statistic calculated in the last step of the variable selection are discussed with reference to the excluded variables. For the final models, the estimated regression coefficients of the selected explanatory influences with respective 95% confidence intervals and p values of the t statistic and the adjusted R^2 are given. All analyses are regarded as explorative, and p values are given descriptively. Therefore, no significance level is fixed.

Results

We evaluated FC (Fig. 1) and body composition (Fig. 2) in patients with tumours or malformations of the sellar region using FMH, a standardized questionnaire, for self-assessment of FC and by calculating BMI SDS. The aim of the study was to analyze the impact of different tumour localization and diagnosis on FC and the degree of obesity in patients during follow-up. Patient groups were comparable in terms of sex distribution, age at diagnosis and last follow-up and the rate of irradiation (Table 1).

One hundred and sixty patients could be evaluated to assess the influence of gender, irradiation, diagnosis, tu-

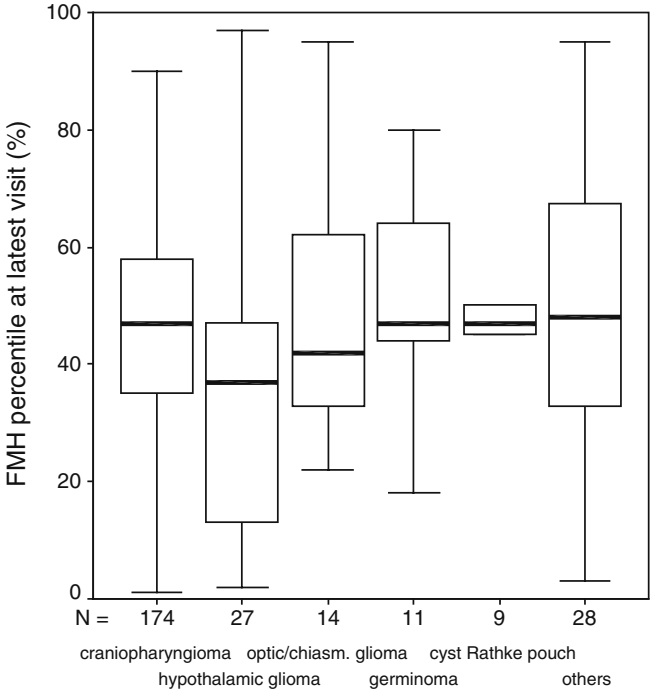

Fig. 1 Descriptive statistics of functional capacity (*FC*) in patients with sellar masses: box plots of percentiles on Fertigkeitenskala Münster–Heidelberg (*FMH*) ability score in patients with childhood craniopharyngioma, germinoma, optic/chiasmatic glioma, hypothalamic glioma, cysts of Rathke's cleft and patients with other sellar masses at the time of latest visit. The *horizontal line* in the middle of the box depicts the median. *Edges* of the box mark the 25th and 75th percentile. *Whiskers* indicate the range of values that fall within 1.5 box lengths

mour localization, hypothalamic tumour involvement, age at diagnosis, age at latest evaluation and time from diagnosis to latest evaluation on FC. Only age at diagnosis and hypothalamic involvement had relevant impact on FC. Involvement of the intrasellar area, craniopharyngioma and cysts of Rathke's cleft did not prove to be explanatory influences on FC in the final step of the variable selection with p values 0.114, 0.133 and 0.193, respectively. All other excluded variables had even larger p values (>0.250). The final general linear model could be built with 209 cases. The FMH score increased 1.48% (95% CI, 0.84–2.11%; p value<0.001) per year of age at diagnosis. Hypothalamic involvement caused a decrease of 8.63% (95% CI, 2.63–14.62%; p value=0.005) in FMH score. The intercept was 31.22 (95% CI, 24.73–37.72; p value<0.001). The adjusted R^2 for the model was 13.4%.

One hundred and ninety-seven patients could be evaluated to assess the influence of gender, irradiation, diagnosis, hypothalamic tumour involvement, tumour localization, age at diagnosis, age at evaluation and time from diagnosis to evaluation on BMI at the latest evaluation. Only BMI at the time of diagnosis, hypothalamic involvement and craniopharyngioma proved to be influential on BMI at the latest evaluation. Involvement of the retrosellar area showed no evidence to be an explanatory influence in the last step of the variable selection (p value=0.154). All other excluded variables had even larger p values (>0.350). The final general linear model could be built with 207 cases. Interaction between hypothalamic involvement and craniopharyngioma just barely failed inclusion in the model (p value=0.075). The BMI SDS at the latest evaluation increased 0.64 (95% CI, 0.49–0.78; p value<0.001) per BMI SDS at diagnosis. Hypothalamic involvement caused an increase of 1.87 (95% CI, 1.22–2.52; p value<0.001) in BMI SDS at the latest evaluation. Patients with craniopharyngioma showed a 0.95 (95% CI, 0.31–1.59; p value=0.004) enlarged BMI SDS at the latest evaluation compared to other tumours of the sellar area. The intercept was 3.31 (95% CI, 2.77–3.84; p value<0.001). The adjusted R^2 for the model was 42.9%.

Although the rate of irradiation was higher in the groups of patients with craniopharyngioma, pilocytic astrocytoma and optic glioma, irradiation did not contribute to differences in self-estimation of FC.

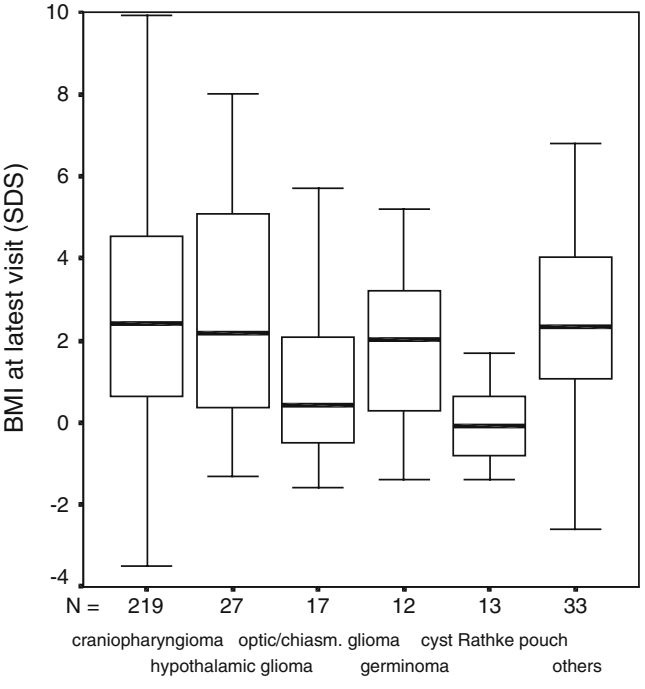

Fig. 2 Descriptive statistics of body composition [body mass index (*BMI*)] in patients with sellar masses: box plots of BMI SDS according to the references of Rolland-Cachera et al. [11] in patients with childhood craniopharyngioma, germinoma, optic/chiasmatic glioma, hypothalamic glioma, cysts of Rathke's cleft and patients with other sellar masses at the time of latest visit. The *horizontal line* in the middle of the box depicts the median. *Edges* of the box mark the 25th and 75th percentile. *Whiskers* indicate the range of values that fall within 1.5 box lengths. One patient with childhood craniopharyngioma presenting with a BMI of 19.5 SD at latest visit is not included in the graph

Table 1 Characteristics in 403 children and adolescents with sellar masses [276 craniopharyngioma, 14 germinoma, 21 optic/chiasmatic glioma, 40 hypothalamic glioma, 13 cysts of Rathke's pouch and 39 other sellar masses (four pituitary adenoma, three prolactinoma, four hypothalamic hamartoma, 15 suprasellar arachnoidal cyst, five central nervous system Langerhans cell histiocytosis, four sarcoma of the basal skull, four pituitary malformations)] who were evaluated for functional capacity by Fertigkeitenskala Münster–Heidelberg ability scale and body composition by body mass index SDS according to the references of Rolland-Cachera et al. [11]

	Craniopharyngioma	Hypothalamic glioma	Optic/chiasmatic glioma	Germinoma	Suprasellar cyst	Cyst of Rathke's pouch	Others
Number	276	40	21	14	15	13	24
Sex (female/male)	136/140	24/16	8/13	7/7	5/10	5/8	10/14
Age at diagnosis (years)	9.0 (0.05–18.0)	3.8 (0.5–18.0)	4.9 (0.7–10.7)	10.9 (7.4–14.7)	5.8 (0.3–12.6)	10.4 (3.3–15.1)	6.1 (0.3–17.7)
Age at evaluation (years)	15.3 (2.3–42.9)	9.6 (1.3–24.4)	8.2 (4.4–17.0)	12.9 (9.4–18.8)	10.1 (0.3–19.7)	13.6 (4.9–21.2)	14.1 (3.4–27.6)
Follow-up interval (years)	5.6 (0–33.7)	3.7 (0.5–14.0)	4.4 (0.9–13.2)	3.5 (0.2–8.1)	2.8 (0–14.1)	3.6 (0–14.7)	5.8 (0.8–10.8)
Irradiation (yes/no)	73/166	10/21	1/17	9/2	0	1/12	7/12
Hypothalamic involvement (yes/no)	125/87	40/0	0/21	6/8	2/13	0/13	7/17

Medians and ranges are shown

Discussion

The assessment of FC and QoL in survivors of childhood intracranial tumours is an important field of research, which is relevant for a better understanding of how affected children feel and how treatment can be optimized [14]. In spite of high overall survival rates reported in the literature [1, 4, 15], patients with tumours of the sellar region frequently suffer from severe sequelae due to endocrine and neurological deficiencies. Recently published studies [4, 16, 17] indicated that in patients with childhood craniopharyngioma, severe obesity due to hypothalamic involvement had a major impact on FC. Furthermore, FC deteriorated in patients with hypothalamic involvement of childhood craniopharyngioma [18].

Hypothalamic lesions, especially in ventromedial areas, are postulated as pathogenic factors for hyperphagia and obesity in affected patients with craniopharyngioma [19]. The regulative influence of the ventromedial and lateral hypothalamus on eating behaviour has been confirmed in animal models [20]. Deficient modulation of hunger in lateral hypothalamic areas due to a lack of feedback caused by lesions in areas of satiety regulation in lateral hypothalamus was postulated as a mechanism for hypothalamic obesity [21]. This neuroanatomical model of pathogenesis in hypothalamic obesity was successively modified by observations on the regulative impact of neurochemical factors as neurotransmitters, neuromodulators and peripheral hormones on eating behaviour. Roth et al. [22] reported on an up-regulation of leptin levels due to an impaired hypothalamic responsiveness caused by craniopharyngiomas with extension to the suprasellar area.

Recent reports in the literature on QoL and FC in survivors of sellar or suprasellar masses are either confined to adult cohorts [15, 22] or to patients with distinct tumour entities at childhood age [23–27] and adult age [28–30]. The results of our comparative analysis support reports on a major negative impact of hypothalamic involvement on QoL and FC in childhood patients with sellar masses [5, 8, 9]. Habrand et al. [24] found a similar trend towards lower QoL in young infants with craniopharyngioma, which, however, did not reach statistical significance.

With regards to reports on QoL in cohorts with distinct tumour entities, the results of our comparative study lead to the assumption that the tumour diagnosis itself reached no specific nor explanatory influence on FC in multivariate analysis. Furthermore, obesity had no explanatory negative impact on FC when analyzed for children and adolescents with different sellar masses.

In paediatric cohorts of patients with germ cell tumours, a high rate of late effects, particularly in patients who received irradiation, has been demonstrated [25]. Neuropsychological sequelae have been reported minimal by others [26] with good overall functional results. Children with optic pathway/hypothalamus gliomas have a good long-term prognosis with a 10-year overall survival of more than 85%. However, severe impairment of FC in these patients was caused by visual and endocrine deficits. In patients with hypothalamic involvement, diencephalic syndrome resulting in cachexia had a major impact on FC and prognosis. Kasperbauer et al. [31] retrospectively evaluated the daily activity of 29 adult patients with cysts of Rathke's pouch. They found that the ability to perform the activities of daily life was normal after surgical management of cysts of

Rathke's pouch. The outcome and FC in children with CNS LCH were impaired in 13% of patients due to reading capabilities below average, in 7% due to mathematical capabilities below average and in up to 40% of patients due to social or behavioural problems [32]. Grois et al. [33] reported on severe impairment of FC in patients with neurological sequelae due to CNS LCH. Based on retrospective evaluation of 11 cases with hypothalamic hamartoma and a review of 61 reported cases of hamartoma in the literature, Arita et al. [34] observed a close relationship between clinical outcome and localization of the hypothalamic hamartoma. In patients with hamartoma of parahypothalamic localization, precocious puberty mainly occurred, whereas in patients with intrahypothalamic localization, FC was severely impaired by developmental delay and seizures. The close relation between severity of seizures and cognitive and psychosocial abilities was also confirmed by other reports [35, 36]. Reports on the specific impact of suprasellar arachnoidal cysts on FC in affected children and adolescents are rare. Di Rocco and Caldarelli [37] reviewed the literature on sequelae in patients with suprasellar arachnoidal cysts. The superior and posterior expansion of suprasellar arachnoidal cysts was reported to induce a stretching and eventual disruption of the pituitary stalk and a compression of the inferomedial portions of the thalami, the tuber cinereum and the mammillary bodies, thus explaining the endocrine dysfunction that was reported in a significant percentage of affected subjects. Sundaram et al. [38] analyzed the pathological findings and clinical course in 145 children and adults with cysts of the CNS, including 23 arachnoidal cysts. Sequelae and prognosis were related to local pressure effects of cystic structures.

Severe obesity and reduced FC due to hypothalamic disorders are major adverse late effect in children and adolescents with craniopharyngioma. Comparable with other reports in the literature [1, 4], the rate of severe obesity was about 40% in our cohort of craniopharyngioma patients. In our comparative analysis of patients with sellar masses, we could confirm that the diagnosis of craniopharyngioma was a major risk factor for obesity, especially in patients with hypothalamic involvement of craniopharyngioma.

Our results support recent observations [4] that patients at risk for severe postoperative obesity had a higher BMI SDS already at the time of diagnosis of childhood craniopharyngioma. This observation supports the hypothesis that the pathogenic mechanisms for obesity due to craniopharyngioma are of early influence in the course of the disease. The observation that a major increase in weight occurred during the early postoperative period [4] supports the postulation that efforts on weight control should be initiated early for patients at risk for severe obesity.

There are several reports [39–48] on neuropsychological and neurobehavioural outcome in children with craniopharyngioma. However, the interpretation is limited because of the small size of cohorts. We were able to demonstrate that young age at the time of diagnosis and hypothalamic involvement of craniopharyngioma were relevant risk factors for an impairment of FC in patients with childhood craniopharyngioma. To improve sequelae, we therefore suggest that in patients at risk, i.e. young infants with craniopharyngioma involving hypothalamus, rehabilitative efforts should be intensified.

However, the rather low explanatory value (R^2=0.134) of our prediction model for FC in patients with sellar masses leads to the suggestion that further analyses on relevant risk factors for QoL and FC in these patients are warranted.

Conclusions

We conclude that hypothalamic tumour involvement and young age at diagnosis have a major impact on FC in children and adolescents with tumours and malformations of the sellar region. We found that impairment of FC was not specifically related to a distinct tumour entity. Rather, the tumour localization and the involvement of hypothalamic structures both had major influence on sequelae. Risk factors for obesity can be identified based on anthropometrical parameters already evaluable at the time of diagnosis. Further analyses on relevant risk factors for the development of obesity in these patients are part of the German prospective multicenter study [10], Kraniopharyngeom 2000, on patients with childhood craniopharyngioma (http://www.kraniopharyngeom.de). Given the potential impact of neuropsychological and neurobehavioural problems on FC and QoL, the prospective study includes a standardized neuropsychological assessment.

Acknowledgements The authors are grateful to M. Neff-Heinrich for her kind support in editing the manuscript. This work was supported by the Deutsche Kinderkrebsstiftung, Bonn, Germany (http://www.kinderkrebsstiftung.de), Grant No. DKS2001, awarded to Hermann L. Müller, M.D., and in part presented at the 85th Annual Meeting of the Endocrine Society 2003, Philadelphia, PA, USA.

References

1. Einhaus SL, Sanford RA (1999) Craniopharyngiomas. In: Albright AL, Pollack IF, Adelson PD (eds) Principles and practice of pediatric neurosurgery. Thieme, New York, pp 545–562
2. Bunin GR, Surawicz TS, Witman PA, Preston-Martin S, Davis F, Bruner JM (1998) The descriptive epidemiology of craniopharyngioma. J Neurosurg 89:547–551
3. Müller-Scholden J, Lehrnbecher T, Müller HL, Bensch J, Hengen RH, Sörensen N, von Stockhausen HB (2001) Radical surgery in a neonate with craniopharyngioma. Pediatr Neurosurg 33:265–269

4. Müller HL, Bueb K, Bartels U, Roth C, Harz K, Graf N, Korinthenberg R, Bettendorf M, Kühl J, Gutjahr P, Sörensen N, Calaminus G (2001) Obesity after childhood craniopharyngioma—German multicenter study on preoperative risk factors and quality of life. Klin Padiatr 213:244–249
5. Rajan B, Ashley S, Gorman C, Jose CC, Horwich A, Bloom HJG, Marsh H, Brada M (1993) Craniopharyngioma—long-term results following limited surgery and radiotherapy. Radiother Oncol 26:1–10
6. Roth C, Lakomek M, Müller HL, Harz KJ (2002) Obesity in children—etiology and treatment. Monatsschr Kinderheilkd 150:329–336
7. De Vile CJ, Grant DB, Hayward RD, Kendall BE, Neville BG, Stanhope R (1996) Obesity in childhood craniopharyngioma: relation to post-operative hypothalamic damage shown by magnetic resonance imaging. J Clin Endocrinol Metab 81:2734–2737
8. Müller HL, Heinrich M, Bueb K, Etavard-Gorris N, Gebhardt U, Kolb R, Sörensen N (2003) Perioperative dexamethasone treatment in childhood craniopharyngioma—influence on short-term and long-term weight development. J Exp Clin Endocrinol Diabetes 111:330–334
9. Müller HL, Schneider P, Bueb K, Etavard-Gorris N, Gebhardt U, Kolb R, Sörensen N (2003) Volumetric bone mineral density in patients with childhood craniopharyngioma. J Exp Clin Endocrinol Diabetes 111:168–173
10. Müller HL, Sörensen N (2001) Kraniopharyngeom 2000—prospective, multicenter surveillance study of children and adolescents with craniopharyngioma. Universitätsverlag Aschenbeck & Isensee, Oldenburg (http://www.kraniopharyngeom.de)
11. Rolland-Cachera MF, Cole TJ, Sempé M, Tichet J, Rossignol C, Charraud A (1991) Body mass index variations: centiles from birth to 87 years. Eur J Clin Nutr 45:13–21
12. Wolff JEA, Däumling E, Dirksen A, Dabrock A, Hartmann M, Jürgens H (1996) Munster Heidelberg abilities scale—a measuring instrument for global comparison of illness sequelae. Klin Padiatr 208:294–298
13. Kosch A, Mölenkamp G, Däumling E, Dirksen A, Jürgens H, Wolff J (1998) Assessment of independence in daily life in pediatric oncology by FMH-questionnaire. Klin Padiatr 210: 390–394
14. Calaminus G, Weinspech S, Teske C, Göbel U (2000) Quality of life in children and adolescents with cancer. First results of an evaluation of 49 patients with the PEDQOL questionnaire. Klin Padiatr 21:211–215
15. Honegger J, Barocka A, Sadri B, Fahlbusch R (1998) Neuropsychological results of craniopharyngioma surgery in adults: a prospective study. Surg Neurol 50:19–28
16. Müller HL, Handwerker G, Wollny B, Sörensen N (2002) Melatonin secretion and increased daytime sleepiness in childhood craniopharyngioma patients. J Clin Endocrinol Metab 87:3993–3996
17. Müller HL, Faldum A, Etavard-Gorris N, Gebhardt U, Oeverink R, Kolb R, Sörensen N (2003) Functional capacity, obesity and hypothalamic involvement—cross-sectional study on 212 patients with childhood craniopharyngioma. Klin Pädiatr 215:310–314
18. Müller HL, Bruhnken G, Emser A, Faldum A, Etavard-Gorris N, Gebhardt U, Kolb R, Sörensen N (2005) Longitudinal study on quality of life in 102 survivors of childhood craniopharyngioma. Childs Nerv Syst (in press)
19. Flynn FG, Cummings JL, Tomiyasu U (1988) Altered behavior associated with damage to the ventromedial hypothalamus: a distinctive syndrome. Behav Neurol 1:49–58
20. Albert DJ, Petrovic DM, Jonik RH, Walsh ML (1991) Enhanced defensiveness and increased food motivation each contribute to aggression and success in food competition by rats with medial hypothalamic lesions. Physiol Behav 49:13–19
21. Blundell JE (1990) Appetite disturbance and the problems of overweight. Drugs 39:1–19
22. Roth C, Wilken B, Hanefeld F, Schröter W, Leonhardt U (1998) Hyperphagia in children with craniopharyngioma is associated with hyperleptinemia and a failure in the downregulation of appetite. Eur J Endocrinol 138:89–91
23. Gsponer J, De Tribolet N, Deruaz JP, Janzer R, Uske A, Mirimanoff RO, Reymond MJ, Rey F, Temler E, Gaillard RC, Gomez F (1999) Diagnosis, treatment, and outcome of pituitary tumors and other abnormal intrasellar masses. Retrospective analysis of 353 patients. Medicine 78:236–269
24. Habrand JL, Ganry O, Couanet D, Rouxel V, Levy-Piedbois C, Pierre-Kahn A, Kalifa C (1999) The role of radiation therapy in the management of craniopharyngioma: a 25-year experience and review of the literature. Int J Radiat Oncol Biol Phys 44:255–263
25. Hale GA, Marina NM, Jones-Wallace D, Greenwald CA, Jenkins JJ, Rao BN, Luo X, Hudson MM (1999) Late effects of treatment for germ cell tumors during childhood and adolescence. J Pediatr Hematol/Oncol 21:115–122
26. Kiltie AE, Gattamaneni HR (1995) Survival and quality of life of paediatric intracranial germ cell tumour patients treated at the Christie hospital, 1972–1993. Med Pediatr Oncol 25:450–456
27. Merchant TE, Kiehna EN, Sanford RA, Mulhern RK, Thompson SJ, Wilson MW, Lustig RH, Kun LE (2002) Craniopharyngioma: the St. Jude children's research hospital experience 1984–2001. Int J Radiat Oncol Biol Phys 53:533–542
28. Saeki N, Murai H, Kubota M, Fujimoto N, Yamaura A (2001) Long-term Karnosfky performance status and neurological outcome in patients with neurohypophyseal germinomas. Br J Neurosurg 15:402–408
29. Sutton LN, Radcliffe J, Goldwein JW, Phillips P, Janss AJ, Packer RJ, Zhao H (1999) Quality of life of adult survivors of germinomas treated with craniospinal irradiation. Neurosurgery 45:1292–1297
30. Villani RM, Tomei G, Bello L, Sganzerla E, Ambrosi B, Re T, Barilari MG (1997) Long-term results of treatment for craniopharyngioma in children. Childs Nerv Syst 13:397–405
31. Kasperbauer JL, Orvidas LJ, Atkinson JL, Abboud CF (2002) Rathke's cleft cyst: diagnostic and therapeutic considerations. Laryngoscope 112:1836–1839
32. Simms S, Warner NJ (1998) A framework for understanding and responding to the psychosocial needs of children with Langerhans cell histiocytosis and their families. Hematol/Oncol Clin North Am 12:359–367
33. Grois N, Tsunematsu Y, Barkovich AJ et al (1994) Central nervous system disease in Langerhans cell histiocytosis. Br J Cancer 70:S24–S28
34. Arita K, Ikawa F, Kurisu K, Sumida M, Harada K, Uozumi T, Monden S, Yoshida J, Nishi Y (1999) The relationship between magnetic resonance imaging findings and clinical manifestations of hypothalamic hamartoma. J Neurosurg 91:212–220
35. Frattali CM, Liow K, Craig GH, Korenman LM, Makhlouf F, Sato S, Biesecker LG, Theodore WH (2001) Cognitive deficits in children with gelastic seizures and hypothalamic hamartoma. Neurology 57:43–46

36. Mottolese C, Stan H, Bret P, Berlier P, Lapras C (2001) Hypothalamic hamartoma: the role of surgery in a series of eight patients. Childs Nerv Syst 17:229–236
37. Di Rocco C, Caldarelli M (1993) Suprasellar arachnoidal cysts. In: Raimondi AJ, Choux M, Rocco CD (eds) Intracranial cyst lesions. Springer, Berlin Heidelberg New York, pp 113–128
38. Sundaram C, Paul TR, Raju BV, Ramakrishna Murthy T, Sinha AK, Prasad VS, Purohit AK (2001) Cysts of the central nervous system: a clinicopathologic study of 145 cases. Neurol India 49:237–242
39. Anderson AC, Wilkening GN, Filley CM, Reardon MS, Kleinschmidt-DeMasters BK (1997) Neurobehavioral outcome in pediatric craniopharyngioma. Pediatr Neurosurg 26:255–260
40. Becker G, Kortmann RD, Skalej M, Bamberg M (1999) The role of radiotherapy in the treatment of craniopharyngioma—indications, results, side effects. In: Wiegel T, Hinkelbein T, Brock M, Hoell T (eds) Controversies in neuro-oncology. Front Radiat Ther Oncol, vol 33. Karger, Basel, pp 100–113
41. De Vile CJ, Grant DB, Hayward RD, Stanhope R (1996) Growth and endocrine sequelae of craniopharyngioma. Arch Dis Child 75:108–114
42. Fisher PG, Jenab J, Goldthwaite PT, Tihan T, Wharam MD, Foer DR, Burger PC (1998) Outcomes and failure patterns in childhood craniopharyngiomas. Childs Nerv Syst 14:558–563
43. Ono N, Kohga H, Zama A, Inoue HK, Tamura M (1996) A comparison of children with suprasellar germ cell tumors and craniopharyngioma: final height, weight, endocrine, and visual sequelae after treatment. Surg Neurol 46:370–377
44. Riva D, Pantaleoni C, Devoti M, Saletti V, Nichelli F, Giorgi C (1998) Late neuropsychological and behavioral outcome of children surgically treated for craniopharyngioma. Childs Nerv Syst 14:179–184
45. Weiner HL, Wisoff JH, Rosenberg ME, Kupersmith MJ, Cohen H, Zagzag D, Shiminski Maher T, Flamm ES, Epstein FJ, Miller DC (1994) Craniopharyngiomas: a clinicopathological analysis of factors predictive of recurrence and functional outcome. Neurosurgery 35:1001–1010
46. Weissenberger AA, Dell ML, Liow K, Theodore W, Frattali, Hernandez D, Zametkin AJ (2001) Aggression and psychiatric comorbidity in children with hypothalamic hamartomas and their unaffected siblings. J Am Acad Child Adolesc Psych 40:696–703
47. Yasargil MG, Curcic M, Kis M et al (1990) Total removal of craniopharyngiomas. Approaches and long-term results in 144 patients. J Neurosurg 73:3–11
48. Van Effenterre R, Boch AL (2002) Craniopharyngioma in adults and children: a study of 122 surgical cases. J Neurosurg 97:3–11