

Postural sway in children and young adults, survivors of CNS tumours

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ABSTRACT

Purpose: Brain tumours are the most common solid tumours in children and adolescents. The increasing survival rate of these patients makes their follow-up and quality of life assessment an important task. The evaluation of the negative influence of anti-cancer treatment on their balance is the aim of this study.

Material and Methods: The balance assessment was performed on patients who completed the treatment of CNS tumours and were disease-free at the time of the study. Eighty-eight patients aged 5 to 24 years participated in the study. Postural sway was recorded using Kistler force plate. Balance test parameters from two conditions: eyes open and eyes closed were calculated and compared with reference data. The severity of the balance disorders was scored for both conditions.

Results: The balance disorders were generally not dependent on the localisation of the tumour. Only patients treated for posterior fossa tumours had a higher score (indicating pronounced balance deficit) in eyes closed condition comparing to others. The patients treated for spinal cord tumours seemed to have increased total sway path in comparison to others. The severity of the balance deficits tended to diminish in time.

Conclusions: These results suggest that the repair mechanisms of the CNS could overcome the problems inflicted by the illness and therapy.

Key words: balance deficits, CNS tumours, children and adolescents, sway, tumour localisation

INTRODUCTION

Brain tumours are the most common solid tumours in children, and the third leading cause of death in children and adolescents younger than 16 years of age [1]. The incidence of the CNS tumours is approximately 27 per 1 million of children younger than 19 years [2]. It is the second common type of cancer after leukaemia in children and adolescents.

Among methods used in the treatment of CNS tumours radiation therapy is regarded as the most detrimental factor of late-effects [2]. Patients suffer from losses in IQ scores, as they are not able to learn in normal pace any longer, endocrine dysfunctions, and even decreased bone mineral density.

The constant increase of survival rate of children suffering from cancer makes their follow-up a very important task. The main aim is to assess the late-effects of anticancer treatment, its negative impact on health status of the cured patients, as

well as evaluation of the patients' quality of life. There are several scales used in such follow-ups, like for example LENT (for assessment of radiation-induced late-effects), or scales evaluating risk connected with neurosurgery or chemotherapy [3]. Balance disorders are one of the main problems limiting daily activities in children and adolescents [4]. Motor system has to deal with a wide variety of perturbations in order to maintain the proper body posture and balance. Such task requires from the central nervous system (CNS) proper selection of motor program (muscle activation pattern) depending on the magnitude and type of the perturbation and biomechanical constraints [5]. Keeping proper maintenance of the balance during standing is a complex process, which involves sensory systems (visual, vestibular, proprioceptive), and requires from the CNS the ability to properly integrate all these information, and to control the efferents [6]. CNS tumours and its complex treatment could negatively influence

the CNS ability in this area. Therefore the aim of the present study was to evaluate the balance tests performed in the CNS tumours survivors. The dependence of the balance deficits on the tumour localisation, age at the illness onset and the time elapsed between the end of the treatment and time of the study was assessed.

MATERIAL AND METHODS

Participants

Eighty-eight patients (33 girls and 55 boys) aged 5 to 24 years participated in the study. All patients were treated of CNS tumours in Dept. of Oncology, The Children's Memorial Health Institute. The patients were divided into six subgroups, depending on the localisation of the tumours. The first subgroup comprised 38 patients with posterior fossa tumours (PF), 17 patients had midline tumours (MID), 10 patients had left (LH) and 9 right hemisphere tumours (RH), 7 patients had brain stem tumours (STEM), 5 spinal cord tumours (SC). In the evaluated group there was also one patient with posterior fossa and spinal cord tumour and one patient with multiple tumours. The balance test results of these two patients were excluded from part of the analysis.

All patients underwent complex (combined) treatment (neurosurgery, followed by chemotherapy and radiotherapy). Among 88 patients 44 were diagnosed with Medulloblastoma/PNET, 24 with glioma, 12 with anaplastic ependymoma and 3 other (atypical rhabdoid teratoid tumor, chordoma, sarcomatous meningioma.)

Patients with MB/PNET received preradiation chemotherapy consisting of cytoxan, vincristine, etoposide alternating with cisplatin, vincristine and etoposide and 8 courses of maintenance chemotherapy of cisplatin, etoposide, vincristine, lomustine. Patients with low grade gliomas received chemotherapy with carboplatin and vincristine and the ones with high grade gliomas cisplatin, vincristine and etoposide or cisplatin and temozolomide.

The treatment was completed before the time of the study: all children were disease free at the time of the study. This was confirmed by laboratory data, CT and MRI scans. The age at the onset of the illness, and the time, which elapsed between the end of the treatment and the time to the study, were noted for each patient.

Patients were recruited for the study from the Outpatient Clinic where they have regular check-ups. The following inclusion criteria were used:

- patients underwent the combined oncological treatment (some CNS tumours patients received only neurosurgery in case of non-malignant tumours – these patients were excluded from the study);
- patients were disease-free.

No other criteria were used, all patients fulfilling above criteria, visiting the Clinic in 2003 to 2006 years were asked

to participate in the study, and no special subject sampling procedure was used. The Ethical Committee approval was obtained prior to the study.

Methods

Balance tests were performed on a Kistler force plate. The centre of pressure trajectory (COP sway) was recorded during quiet standing on the force plate for 50 to 60 s. There were two trials: one with eyes opened and the second with eyes closed. Data were collected at 60 Hz, and the data from the middle 30 s were taken for further analysis. During the data collection children were assisted by the laboratory staff to ensure their safety, but were not held by them. Only one patient (with multiple tumours) was unable to finish the balance test in eyes closed condition. The own MATLAB procedure was used to calculate the following parameters from the COP sway: maximum radius of sway, mean radius of sway, total sway path during 30 s, maximum left and right displacements, and maximum fore and aft displacements. The results of the patients were compared with reference values of healthy children [7, 8].

The results of the balance trials were additionally scored, separately for eyes closed and eyes opened. The following scale was adopted: 0 – all results were within normal range, 1 – total sway path was increased, 2 – total sway path and one or two other variables were increased – 3 – more than four variables were increased.

Statistical methods

The qualitative data were compared using Pearson chi-square test. The distribution of the parameters was checked either with Kolmogorov-Smirnov and Shapiro-Wilks tests (comparison with normal distribution) or Kolmogorov-Smirnov and chi-square tests (log-normal distribution). As all variables were log-normally distributed therefore the ANOVA Kruskal-Wallis was used for further comparisons.

RESULTS

The statistical analysis revealed that there was no statistical difference in any of the variables between the groups, neither in eyes open, nor in eyes closed condition. *Tab. 1* summarizes the results for eyes open condition, and *Tab. 2* for eyes closed condition.

In eyes open condition there was no statistical difference between the groups in the obtained scores ($\chi^2=21.518$, $df=15$, $p=0.121$), in contrast to the eyes closed condition ($\chi^2=27.679$, $df=15$, $p=0.024$). When patients treated of posterior fossa tumours were excluded from the comparison there was no statistical differences between the groups. *Tab. 3* presents the scores in different groups in eyes open condition, and *Tab. 4* in eyes closed condition. *Tab. 5* presents the age at the onset of the illness in the groups,

Table 1. The results of the eyes open balance test, and the comparison of the variables between the groups. The variables are summarized by the geometric means and range [mm]. NS- statistically non significant.

Variable	PF	RH	MID	SC	LH	STEM	Comparison
Max radius	22.4 5.7-50.7	23.1 3.2-107.1	21.4 8.0-94.1	30.2 11.9-126.1	21.0 8.1-58.8	19.4 12.7-47.7	NS
Mean radius	7.4 2.6-15.3	6.6 3.2-10.5	5.6 2.7-12.6	7.3 3.2-11.9	6.4 2.6-30.0	6.0 2.8-21.6	NS
Total path	658.1 372.7-1647.3	653.0 227.2-2030.0	508.5 191.0-1502.8	1008.8 501.6-2366.3	520.5 273.6-907.0	530.7 316.2-1146.3	NS
Max left	14.2 3.8-45.1	17.9 6.3-74.4	12.6 3.3-93.4	25.0 5.5-126.1	10.0 2.0-34.4	10.9 4.7-41.3	NS
Max right	16.3 6.0-36.6	17.6 4.5-104.8	12.7 3.0-56.8	21.3 9.4-38.2	11.4 2.0-33.1	13.1 6.4-43.6	NS
Fore	16.7 7.3-43.7	15.8 7.6-48.7	14.0 5.5-33.2	14.6 5.4-27.1	14.4 7.9-41.1	12.7 7.5-31.2	NS
Aft	16.0 5.6-33.2	12.3 6.6-47.2	13.7 6.6-40.9	17.3 10.6-29.4	17.5 5.9-58.9	13.2 7.7-23.3	NS

Table 2. The results of the eyes closed balance test, and the comparison of the variables between the groups. The variables are summarized by the geometric means and range [mm]. NS- statistically non significant.

Variable	PF	RH	MID	SC	LH	STEM	Comparison
Max radius	27.1 10.8-62.7	30.3 12.4-105.7	19.5 9.9-51.5	28.8 17.5-46.3	27.4 7.9-81.8	19.2 12.8-51.5	NS
Mean radius	8.9 4.5-102.0	8.4 3.6-16.8	6.3 2.7-15.8	14.2 5.3-101.0	6.5 2.4-15.3	6.4 4.1-14.9	NS
Total path	825.2 353.5-3721.3	831.6 427.7-1096.7	529.4 261.6-1291.8	1242.3 615.3-2762.1	686.8 424.7-1276.9	617.9 300.6-2566.7	NS
Max left	16.6 5.1-44.2	23.0 7.4-104.3	12.6 4.5-32.7	18.5 6.7-36.1	15.3 3.4-55.6	14.1 7.2-27.8	NS
Max right	16.4 5.5-60.5	18.9 8.4-36.3	12.2 5.1-46.0	22.4 15.7-31.5	16.6 6.8-65.4	13.5 5.2-36.3	NS
Fore	19.9 8.3-43.7	16.9 7.8-28.2	14.0 6.4-25.8	19.1 10.3-44.8	18.4 7.0-77.9	14.5 6.2-46.5	NS
Aft	19.1 8.0-55.0	17.6 7.4-25.1	13.1 5.8-31.6	20.3 12.9-30.1	17.0 6.6-31.8	14.8 6.5-42.2	NS

and the time, which elapsed between the end of the treatment and time of the study. As the distributions were neither normal nor log-normal the medians and ranges summarized the variables.

The comparison of the age at the onset of the illness revealed statistically significant difference between the groups (H=12.065, p=0.034), but after the removal of the SC group the statistical difference disappeared (H=4.864, p=0.302).

The time, which elapsed between the end of the treatment and the study, was not different between the groups (H=6.032, p=0.303).

The age at the onset and the time span between the end of the treatment and the study, were also compared between the scores, separately for eyes open and eyes closed condition. No differences were found for the age at the illness onset. On the contrary, for the time, which elapsed between the end of the treatment and the study in both conditions, statistically significant differences were found. The results are presented at Fig.1 and Fig.2, and Tab. 6 and Tab. 7.

DISCUSSION

Sway parameters are one of the methods used for assessment of the balance function in humans. This function depends on the number of systems (vestibular, visual, somatosensory), which are developing in children with age. In the literature there are contradictory data concerning the development of postural control with age. Some studies reported the dependency of the sway parameters on age [9-11], but the ontogenic development of the balance was in these papers investigated in very young children. Some studies report that the development of the control strategies of static posture takes place up to 12 years old [12,13], other state that the full development takes place up to 18 years old [14,15]. Taguchi and Tada (after Tsai) [12] found that the spontaneous sway mode in children reach adult levels by 9 to 12 years old in eyes open condition, and by 12 to 15 years old in eyes closed postures. In one study the sex differences were found in balance parameters, with boys

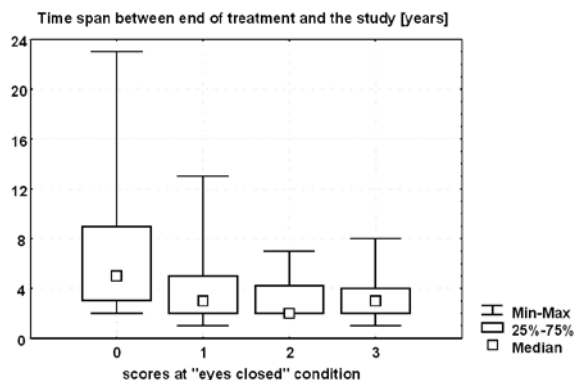
Table 3. Scores during eyes open condition.

	0	1	2	3
PF	8	19	5	5
RH	3	2	3	1
MID	8	6	2	1
SC	0	2	0	3
LH	3	3	3	1
STEM	4	1	1	1

Table 5. Age at the onset and time elapsed between the end of the treatment and the study.

	Age at the onset [years]	Time elapsed [years]
PF	8 <1 – 19>	3.5 <2 – 13>
RH	5 <1 – 14>	5 <1 – 23>
MID	8 <1 – 16>	3 <2 – 11>
SC	3 <2 – 4>	5 <3 – 9>
LH	11 <2 – 15>	4.75 <1 – 8>
STEM	5 <2 – 15>	4 <3 – 16>

Figure 2. Time between the end of the treatment and the study in four score groups. Eyes closed condition.

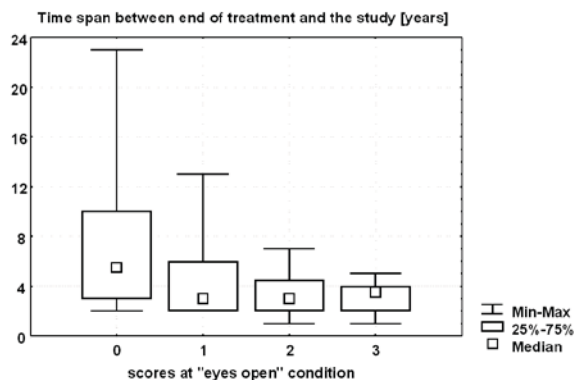


exhibiting greater and faster movements than girls up to 9 to 10 years old [16]. There are also some indications that increased body mass could influence the balance performance. In adult male subjects the weight dependency of COP speed was found [17], while in obese boys the increased maximum displacement of COP in medio-lateral direction was found [18]. In other studies when the balance sway was investigated in older children and adolescents (from 6 to 18 years old) [7, 8, 19, 20] no correlation between the developmental parameters (such as age, body mass or stature) was found both for eyes opened and eyes closed conditions. Thus in these studies the normal ranges of the sway parameters were the same regardless of the stature or age of the subjects, as long as they were at least 6 years of age. Such discrepancy in the data could be explained by the results of a study in which the COP sway parameters were investigated in various strategies. The researchers did not

Table 4. Scores during eyes closed condition.

	0	1	2	3
PF	13	12	5	7
RH	5	1	3	0
MID	11	3	3	0
SC	1	1	0	2
LH	3	4	0	3
STEM	5	0	1	1

Figure 1. Time between the end of the treatment and the study in four score groups. Eyes open condition.



found any direct dependence of COP trajectory and posture on strategy used, while taking into consideration ankles, knees, hips and shoulders [21]. This could indicate that while the control of static posture is still developing after the 6 years of age this fact is not necessarily reflected in changes in sway parameters.

In many clinical studies the sway parameters were compared between healthy and diseased children, regardless of age and body weight. In one study the balance of 11 patients with cerebral palsy (CP) aged 6 to 18 years old were compared with data of 8 healthy children aged 5 to 13 years old [22], in another one data of 23 CP patients were compared with 92 healthy subjects, both groups aged 5 to 18 years old [23]. Gagnon and co-workers compared 40 children aged 7 to 16 years old after mild traumatic brain injury with their healthy counterparts [24].

In the studies of healthy children from which the reference data were taken for comparisons [7, 8] no dependence of age, body stature or body mass was found. Therefore the data of the patients were pooled together, and body stature or age were not used as factors, which could influence the balance sway.

In our group only one patient was below 6 years of age (5 years old), and all other patients were older. The youngest child's sway parameters were within the normal values. Only four children were overweight. They BMI and balance results were presented in Tab. 8. As their results did not differ from other patients they were not excluded from the database. During eyes open condition only 27 patients had all variables

Table 6. Age at the onset of the illness and time elapsed between the end of the treatment and end of the study in groups of patients scored in eyes open condition. NS- statistically non significant.

	0	1	2	3	Comparison
Age at onset	9 <1 – 19>	7 <1 – 16>	7.5 <1 – 14>	4.5 <2 – 16>	NS
Time elapsed	5.5 <2 – 23>	3 <2 – 13>	3 <1 – 7>	3.5 <1 – 5>	H=12.228, p=0.007

Table 7. Age at the onset of the illness and time elapsed between the end of the treatment and end of the study in groups of patients scored in eyes closed condition. NS- statistically non significant.

	0	1	2	3	Comparison
Age at onset	8 <1-16>	7.5 <1 – 15>	5.5 <1 – 19>	7 <1 – 16>	NS
Time elapsed	5 <2 – 23>	3 <1 – 13>	2 <2 – 7>	3 <1 – 8>	H=13.412, p=0.004

Table 8. Obese children data. As BMI changes during development the patients BMI was normalized on BMI of healthy Polish children of appropriate sex and age group [29].

Patient	BMI[kg/m ²]	Normalized BMISDS	Balance score eyes open	Balance score eyes closed
1	32.6	7.0	0	0
2	30.3	3.23	0	1
3	22.6	4.64	2	0
4	36.14	6.83	1	0

within normal range, and during eyes closed condition 34 patients. Most patients had balance problems in both conditions, which suggests that in their case the visual feedback was not sufficient to compensate for the balance deficits. Patients who had no balance problems during eyes open condition remained stable during eyes closed condition. Seven patients had better balance control while standing with eyes closed than during eyes open. This result suggests that during eyes closed condition they use a strategy, which increases the stiffness at the leg joints in order to minimize the body excursions.

In approximately half of the patients with balance deficits (in eyes open condition 33 per 61, and in eyes closed 21 per 54) the only increased variable was total sway path of the COP.

This finding suggests that these patients' sense of the body positions and orientation in space (the maximal excursions of the COP were in these patients normal) is intact but they need more corrections to keep their COP within proper region of the base of support.

There were no statistically significant differences in analysed variables between the groups (Tab. 1, Tab. 2), although the total sway path of the SC group seems to be increased. As this group was very small (5 patients) the increase of the number of patients could change the test result: the p-value was very close to the border line (p=0.055). In this group of patients the age at the onset of the illness was lower than in the other groups (Tab. 5). It seems that in patients after spinal cord tumours treatment the eyes closed condition requires more vigorous control of the COP than in other groups. These results suggest that the balance problems in patients after the treatment of CNS tumours do not depend on the localisation of the tumours, except for SC. This finding confirms our preliminary results [25].

The dependence between the scores and the localisation in the eyes open condition was not confirmed by the statistical analysis. In the eyes closed condition in the group of patients treated of posterior fossa tumours there was an increased number of patients who received the worst score in comparison to the other groups. When these patients were excluded from the analysis no dependence was found between the score and localisation. When the patients were divided not according to the localisation of the tumour, but according to the score obtained in eyes open and eyes close condition the statistically significant difference was found for the time, which elapsed between the end of the treatment and time of the study. Patients who received lowest score (0) completed their treatment much earlier than patients who received higher scores. This finding is consistent with our preliminary results [25].

Chemotherapy treatment could influence the execution of the most difficult balance tests in leukaemia patients, as proved by study of Galea et al. [26], but in standard balance test these patients did not differ from their healthy counterparts. In our study a standard balance test was used: quiet standing in two conditions. Approximately only one third of the evaluated patients had no balance deficits, but additionally to chemotherapy our patients had neurosurgery and radiotherapy, two types of treatment, which potentially compromise the CNS function. Our findings suggest that despite the localisation of the tumour in the CNS and the invasive treatments the repair mechanisms could in time overcome the balance deficits. This finding supports the view that the plasticity of the young brain allows CNS' recovery after damage [27].

CONCLUSIONS

Rehabilitation was proven to improve the functional status of cancer survivors suffering from cancer and treatment related impairments [28]. The results from our study suggest that CNS tumour patients balance deficits inflicted by the illness and treatment tend to disappear in time, which suggests that early rehabilitation could result in earlier improvement.

In conclusion approximately one third of the CNS tumour survivors do not suffer from any balance problems. Despite of the localisation of the tumour the plasticity of the nervous system in most cases can overcome in time the balance deficits.

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