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CEREBELLAR TUMOR AND OSTEOGENESIS IMPERFECTA: DIFFERENT PROFILES OF COGNITIVE DECLINE

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Abstract

Currently, clinical psychology pays great attention to the study of cognitive development of children with different physical disabilities, what leads to mental dysontogenesis. However, a small number of studies are devoted to the study of fluid intelligence and executive control functions in children with different types of dysontogenesis. In this study we investigated two types of dysontogenesis: impaired and deficient dysontogenesis. Our work involved 14 children with a history of neoplasms in the posterior cranial fossa and cerebellum, 18 children with osteogenesis imperfecta (OI, characterized by increased fragility of bones) and 18 normatively developing children. It was found that both types of dysontogenesis worsens the level of children's cognitive development. Our study for the first time demonstrates that characteristics of cognitive development decrease also depend on severity of disease. In our study we investigated two OI types. Children with the first type have moderate impairments, children with the third type have severe motor impairments. Results of children with type 3 of OI could be compared to the results of children with neuro-oncology, while cognitive development of children with type 1 of OI is close to normative. The only exception is sequential reasoning skills: they are declined in both types of OI. The correlation between the level of fluid intelligence and the level of executive functions differs depending on the type of dysontogenesis.

Keywords: Cognitive development, deficient development, fluid intelligence, impaired development, oncology, osteogenesis imperfecta.

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1. Introduction

Appearing in early childhood, different somatic desires can cause psychological disorders. In order to provide all necessary help for those children, we need to have clear understanding what psychological features have children with different somatic desires. Classification of such psychological disorders was invented by Lebedinsky (Roschina & Zvereva, 2012). Based on several health indicator (localization and time of the lesion, the presence of primary and secondary defects, the totality and partiality of the central nervous system lesion) this typology describes 6 main variants of mental dysontogenesis: underdevelopment, delayed development, impaired development, deficient development, distorted and disharmonious development (characterized by asynchrony of development). Whether a particular physical disease will have a damaging effect or cause a developmental deficiency depends on the time of the onset of the disease and the localization of the damaging effect. In our work, we will concentrate on the cognitive development of children with impaired development and deficient development.

Impaired development arises if the damaging effect on the central nervous system emerges when significant part of the child's functional systems had already been formed and there was a period of normative development. Deficient development arises when the damaging effect on the central nervous system existed already in perinatal period or appeared in early-age, so the child had no period of normative development without the disease.

The reasons of cognitive decline due to somatic disease are well described in the literature. The first factor is asthenic physical state of the child, which leads to sub depressive emotional state, and decrease of cognitive characteristics (Lebedinsky, 2006). The second factor is drug therapy, which can lead to significant cognitive decline (Burdukova et al., 2015), and can cause conditions such as fatigue or aggression (Kawadler et al., 2016). The third factor is the limitation of the level of physical activity like movement on a wheelchair or prolonged hospitalization. It influences the level of development of social skills and academic performance. These factors can also lead to motivation decrease and other school problems (Pinquart & Teubert, 2012).

Cerebellum tumor and osteogenesis imperfecta have different course of the disease. Due to their characteristics they cause impaired development and deficient development respectively. Osteogenesis imperfecta is congenital metabolic bone disease and belongs to the group of connective tissue disorders. Patients have defects in collagen synthesis (main component of the bones), which causes frequent bone fractures starting from intrauterine period. To date there are distinguished 15 types of osteogenesis imperfecta, all they differ by severity of the disease. Our focus of attention will be on type I and type III. Type I is characterized by mild disease: congenital and early hearing loss, moderate severity of bone changes. Bone fractures mostly happen in early childhood, or at school age (compression fractures of the vertebrae after long seating). Type III is characterized by more serious disease: first bone fractures occur in the perinatal period, this leads to future bone deformities. Usually patients with such diagnosis are not able to walk independently and use wheelchair (Povorozniuk et al., 2009; Ignatovich et al., 2018). One can easily see that this type of disease influence child development throughout his life, so it leads to deficient dysontogenesis. Cancer has completely different clinical picture: it appears at certain time moment, before that children's development occurs normally. The most common cancer types in childhood are leukemia and malignant brain tumors (Volkova et al., 2019), all of them need immediate special treatment. Despite

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the large number of studies which describe effect of chemo- and radiation therapy on the cognitive development, very small amount of studies take into account the localization of tumor (Burdukova et al., 2015; Burdukova et al., 2017a). Recent studies have shown, that tumors in the posterior cranial fossa and cerebellum leads to cognitive decrease, while tumors of the pineal region of the brain and tumors of the parietal and temporal parts of the cortex do not have such effects (Burdukova et al., 2015; Burdukova & Alekseeva, 2016; Burdukova et al., 2017a). In our study we will focus on the impaired development dysontogenesis appeared due to tumor localization.

2. Problem Statement

Based on this question, we put forward our purpose of this study: explore the features of fluid intelligence and cognitive control (as the most important characteristics of the cognitive profile) in two groups of patients: one with the cerebellar tumor and other one with osteogenesis imperfecta.

3. Research Questions

What cognitive characteristics have different types of dysontogenesis?

4. Purpose of the Study

Based on this question, we put forward our purpose of this study: explore the features of fluid intelligence and cognitive control (as the most important characteristics of the cognitive profile) in two groups of patients: one with the cerebellar tumor and other one with osteogenesis imperfecta.

5. Research Methods

5.1. Participants

Fifty children between 10 and 18 years (mean age 15±2.14) contributed data to the present study. The experimental group 1 consisted of 18 children with diagnosis osteogenesis imperfecta Q78.0 (osteogenesis imperfecta, Wrolik syndrome, Lobstein-Wrolik disease). Six of them had first type of osteogenesis imperfecta and eleven had third type. Data was collected on the base of “Fragile People” Charitable Foundation. The control group and the comparison group (experimental group 2) were formed by a pair-to-pair strategy: all subjects in these two groups were equivalent to subjects from the experimental group 1 in age and gender. Experimental group 2 consisted of 14 children (mean age 14.6±2.1) with diagnosis cerebellar tumor undergoing treatment at the Morozov Children's City Clinical Hospital. All children underwent surgery to remove the neoplasm. Nine children underwent neuro-oncological treatment (chemo- / radiotherapy). The control group consisted of 18 typically developing children (mean age 14.7 ± 2.4).

5.2. Fluid Intelligence Measures

Kaufman Assessment Battery for Children, the Second Edition (KABC–II) was used to estimate individuals’ fluid intelligence (Kaufman & Kaufman, 2004). In this study we used four scales: (Sequential/Gsm (short-term memory), Simultaneous/Gv (visual processing), Learning/Glr (long-term

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storage and retrieval), Planning/Gf (fluid reasoning), and global score that emphasizes mental processing, the Mental Processing Index (MPI). Each of the four scales has two subscales. The expanded battery takes about 190 minutes to administer children ages 7 to 18.

5.3. Cognitive control Measures

To assess the development level of executive functions the computer version of the Cambridge Neuropsychological Test Automated Battery (CANTAB) was used. The following two subtests were selected for recent study: Spatial Working Memory (SWM) (assessed spatial working memory and strategy) and working memory Spatial Span (SSP) (assessed spatial working memory span). Two subtests were administered for a total of approximately 25 min to assess the executive function of the recruited patients.

5.4. Data analysis

For statistical data processing, we used one-way analysis of variance for related samples and Spearman's rank correlation coefficient. As dependent variables, scores on Sequential, Simultaneous, Learning, Planning and MPI were taken. Two independent variables in this experiment were the type of dysontogenesis caused by osteogenesis imperfecta or cerebellar tumor. Deficient development variable had two conditions— type I and type III of osteogenesis imperfecta. A STATISTICA 10.0 (StatSoft Inc) software package was used for these calculations.

6. Findings

We registered cognitive development decline in both experimental groups. Table 1 illustrates MPI scale results. We can easily see that both clinical groups have significantly decrease of cognitive development level to compare with typically developing children ($F=12.9$, $p<0.001$). Stronger decline is registered in the case of impaired development ($F=30.066$, $p<0.001$) then in the deficient development group ($F=12.93$, $p<0.001$).

Table 01. Mental processing index results

	Cerebellar tumor	**Osteogenesis imperfecta type I**	**Osteogenesis imperfecta type III**	**Typical development**
MPI scores (mean±st.d)	86.5±15.3	109.2±8.93	91.6±12.5	114.2±6.7

To reveal the difference between type I and type III of osteogenesis imperfecta we applied one way ANOVA. We could see that children with type I are more successful then children with type III ($F=9.29$, $p<0.009$). Therefore we can conclude, that the level of cognitive development in deficient development group depends on the type of imperfect osteogenesis: cognitive development level of children with imperfect osteogenesis type III is very close to cognitive development level of children with impaired development caused by cerebellar tumor, meanwhile cognitive development level of children with imperfect osteogenesis type I is very close to typically developing children ($F=1.72$, $p=0.209$).

Fluid intelligence was also decreased in experimental groups ($F=14.86$, $p<0.001$). Table 2 illustrates results on “Planning” scale and two subtests that constitute it: “Story completion” and “Pattern Reasoning”.

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Table 02. Planning scale results

	Cerebellar tumor	**Osteogenesis imperfecta type I**	**Osteogenesis imperfecta type III**	**Typical development**
Planning scale (mean±st.d)	78±23.2	109.5±7.2	96.5±13.9	114.3±7.6
Story completion (mean±st.d)	6.7±2.9	10.5±3.1	7.7±3.8	11.7±2.4
Pattern reasoning (mean±st.d)	7.8±3.9	12.3±1.8	10±1.8	13.3±2.7

To compare with typically developing children fluid intelligence was more reduced in experimental group with impaired development ($F=11.24$, $p<0.004$) then with deficient development ($F=8.84$, $p<0.007$). It is important to notice, that there is influence of different types of osteogenesis imperfecta on “Planning” scale ($F=8.25$, $p<0.003$). Results on “Planning” scale performed by Children with osteogenesis imperfecta type I don’t differ from typically developing children ($F=1.5$, $p=0.229$) but children’s abilities with osteogenesis imperfecta type III are reduced much to compare with typically developing children and of osteogenesis imperfecta type I ($F=13.92$, $p<0.002$ and $F=4.5$, $p=0.05$, respectively).

In accordance to ANOVA, subtest “Pattern reasoning” is easier than “Story completion” subtest ($F=11.32$, $p<0.005$) for children with osteogenesis imperfecta. However, there is no such difference detected for children with cerebellar tumor.

At this point we could conclude that it is not enough to know the type of dysontogenesis, but also important to keep in mind disease severity. In further analyses, we decided to estimate decrease within other cognitive functions.

Sequential scale scores and two subtests, which constitute it: “Number recall” and “Word order” are presented in Table 3.

Table 03. Sequential scale results

	Cerebellar tumor	**Osteogenesis imperfecta type I**	**Osteogenesis imperfecta type III**	**Typical development**
Sequential scale (mean±st.d)	86.1±15.3	102.5±7.9	88.1±12.94	114.2±10.7
Number recall (mean±st.d)	7.9±3.8	11.7±1.8	8.8±2.6	10.7±2.7
Word order (mean±st.d)	7.3± 1.9	9.2±2.1	7.1±2.4	11.3±1.6

Children with both types of dysontogenesis demonstrate lower scores on “Sequential” scale compared with typically development control group ($F=14.09$, $p<0.001$). Children with deficient development demonstrate significant decrease then typically development children ($F=19.49$, $p<0.001$). Children with impaired dysontogenesis also demonstrated decrease of sequential reasoning compared with control group ($F=10.72$, $p<0.005$) and compared to children from group with osteogenesis imperfecta type I ($F=6.15$, $p<0.03$). It is interesting, that in the case of sequential reasoning skills, children with both types of osteogenesis imperfecta show lower scores then children from control group ($F=15.016$, $p<0.001$ for all groups; $F=5.48$, $p<0.04$ for type I; $F=26.64$, $p<0.001$ for type III). Subtest “Number recall” is easier for

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them then "Word order" (F=10.46, p<0.006), meanwhile there is no such difference for children with the cerebellar tumor.

Learning scale scores and scores of two subtests, which constitute it "Atlantis" and "Rebus" are presented in Table 4.

Table 04. Learning scale results

	Cerebellar tumor	**Osteogenesis imperfecta type I**	**Osteogenesis imperfecta type III**	**Typical development**
Learning scale (mean±st.d)	97.7±14.5	105. 5±9.8	97.6±8.3	104.9±11.3
Atlantis (mean±st.d)	9±2.6	11.7±1.5	10.2±1.7	12.3±2.4
Rebus (mean±st.d)	9.7±3.1	10.3±2.1	9±2.1	12.3±1.3

Children with both types of dysontogenesis have lower scores than children in control group (F=7.78, p<0.003; for impaired development group and deficient development, respectively: F=11.243, p<0.004 and F=10.791, p<0.005). We obtained no difference in subtest performance for children with cerebellar tumor. Subtest "Atlantis" is a bit easier then subtest "Rebus" for children with deficient development (F=4.38, p=0.056). This tendency may be caused by decline of semantic memory function but not associative memory function. On the other hand, these results could be due to their increased fatigue and asthenization. A milder form of the osteogenesis imperfecta type I does not affect the level of associative memory and the ability to learn new skills, only children with osteogenesis imperfecta type III show this decline.

Results for simultaneous scale and two subtests, that constitute it "Rover" and "Block Counting" are presented in Table 5.

Table 05. Simultaneous scale results

	Cerebellar tumor	**Osteogenesis imperfecta type I**	**Osteogenesis imperfecta type III**	**Typical development**
Simultaneous scale (mean±st.d)	90.4±15.5	110.6±15.1	94.9±14.3	113.7±9.3
Rover (mean±st.d)	8±3.6	12.6±1	10±2.6	12.1±1.5
Block counting (mean±st.d)	8.2±2.6	11.3±2.1	9.5±1.9	12±1.8

Children with both types of dysontogenesis have lower scores then children from control group (F=7.33; p<0.003), but for impaired development group this decrease is much stronger (F=18.369, p<0.001) than for deficient development group (F=6.7, p<0.021).

Type of osteogenesis imperfecta affects success rate of "Simultaneous" scale (F=6.584 p<0.006). Children with osteogenesis imperfecta type III demonstrate significant decrease in simultaneous processing abilities compared with typically developing children (F=13.363, p<0.003). Subtest "Rover" is easier than subtest "Block Counting" for children with deficient development (F=4.49, p=0.05), though there was no difference in these subtest scores for children with cerebellar tumor. These results could appear due to

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asthenization of the children from group with deficient development, because subtest “Block Counting” goes after “Rover” subtest. Elseways, this tendency may appear as a result of decline of counting mathematic abilities.

To evaluate the level of executive functions we used the average number of errors in CANTAB subtests. Results for Spatial Working Memory tasks are presented in Table 6.

Table 06. Spatial working memory results

	Cerebellar tumor	**Osteogenesis imperfecta type I**	**Osteogenesis imperfecta type III**	**Typical development**
The average number of errors in the task "4 boxes" (mean±st.d)	0.325± 0.53	0	0.416±0.72	0.15±0.39
The average number of errors in the task "6 boxes " (mean±st.d)	2.35±2.77	1.175±0.672	1.16±2.14	1.45±1.68
The average number of errors in the task "8 boxes " (mean±st.d)	5.675±3.43	3.775±1.44	4.458±4.14	3.1±2.42

Children with both types of dysontogenesis make more errors then children from control group. Children from impaired development experimental group made significantly more errors in more complex tasks ($F=4.63$, $p<0.05$). In deficient development experimental group, we also evaluated the working memory Spatial Span that is defined as amount of visuospatial storage (the length of the most successfully memorized sequence). This data is presented in Table 7.

Table 07. Spatial span results

	Osteogenesis imperfecta type I	**Osteogenesis imperfecta type III**
Working memory spatial span (mean±st.d)	6.1±1.45	7±1.14

Type of deficient development does not influence the executive functions ($F=0.375$, $p=0.55$ for Spatial Working Memory; $F=0.85$, $p=0.37$ for Spatial Span).

We used the Spearman rank correlation coefficient to estimate the relationship between executive functions the level of cognitive development and fluid intelligence. We included following variables in our analysis: the level of general cognitive development, all scales and subtests scores of the KABC–II, and the average number of errors in the spatial working memory test of the CANTAB battery. We obtained results of correlation analysis for two experimental groups. In experimental group I with impaired development,

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we found significant relationship between the planning scale, the simultaneous scale and the parameters of the spatial working memory. This data is presented in Table 8.

Table 08. Correlation between KABC-II scales and spatial working memory presented by CANTAB tasks in children with impaired development

	Planning scale	**Simultaneous scale**
The average number of errors in the task "6 boxes "	–0.79*	–0.69*
The average number of errors in the task "8 s boxes "	–0.72*	–0.74*

Note:* – significance level $p<0.05$

In experimental group I with deficient development, we found significant relationship between Sequential reasoning abilities and spatial working memory. This data is presented in Table 9.

Table 09. Correlation between KABC–II scales and spatial working memory presented by CANTAB tasks in children with deficient development

	Sequential reasoning scale	**Word order subtest**
The average number of errors in the task "6 squares"	–0.56*	–0.67*

Note:* – significance level $p<0.05$

Our data demonstrates that for each type of dysontogenesis spatial working memory capacity differently correlates to KABC–II scales and subtests. We received correlation between fluid intelligence and spatial working memory for children with impaired development. Problems with short term working memory and spatial abilities lead to decrease of fluid intelligence. In addition, these children have difficulties with ability to integrate visual information what correlates with lower level of spatial working memory. Significant correlation between verbal working memory and spatial working memory in the group with deficient development light up problems with all memorization processes.

Our results indicate that children with cerebellar tumor demonstrate a decrease of short-term memory capacity, decrease of spatial and verbal working memory, and decrease of associative memory abilities. Children with both types of osteogenesis imperfecta demonstrate auditory-verbal short-term memory and verbal working impairment.

7. Conclusion

Our study reveals that impaired development and deficient development lead to decline of executive function and level of cognitive development. The level and characteristics of this decline depends on the type of dysontogenesis. The major difference are observed in fluid intelligence profile and Sequential reasoning abilities. Children with impaired development demonstrate uniform decrease across all scales of Fluid intelligence. The reason of Fluid intelligence decrease could be reduced short term memory span (Rzhanova et al., 2018). Meanwhile children with deficient development show more decline in processing verbal information. Story plot understanding is one of the main problems for this group of children. It could be due to physical and social restrictions which have children with osteogenesis imperfecta type III

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(movement in a wheelchair, home schooling, social isolation).These restrictions affect the development of their spatial abilities and social skills (Troitskaya, 2013; Hill, Baird & Walters, 2014). Generally, this leads to decrease in ability to understand social interaction rules and behavior, which are necessary for successful completion of the "Story Completion" subtest.

Children from impaired development group show uniform decrease in Sequential reasoning abilities. This data corresponds with previous studies (Burdukova et al., 2015; Burdukova & Alekseeva, 2016; Burdukova et al., 2017a). Children with deficient development also demonstrate a significant decrease, but they differ in their executive functioning profile. The main problems for this group are related to verbal working memory and visual working memory (Rzhanova et al., 2018).

Spatial and simultaneous abilities are heavily impaired in the group of children with cerebellar tumor. This could be caused by decrease of spatial working memory (Burdukova et al., 2017a). In accordance with recent studies, the main factor affecting spatial abilities in this group of children is chemotherapy and radiation treatment (Burdukova et al., 2015; Burdukova et al., 2017a). Spatial disabilities and problems with simultaneous processing were also detected in the group with osteogenesis imperfecta, but our results show for the first time that degree of decline depends on the type of osteogenesis imperfecta. Type III is characterized by serious movement constraints; children with such diagnosis demonstrate decrease of spatial and mathematic abilities. It could be caused by limitations of motor experience, which is necessary for the right development of spatial functions involved in mathematic abilities. In addition, our data reveals learning abilities declined in both experimental groups. In accordance with previous findings (Burdukova et al., 2015; Burdukova et al., 2017a, 2017b) our study demonstrates that children with impaired development have problems with associative learning and semantic learning abilities, which could be due to their treatment. In osteogenesis imperfecta group spatial abilities decline depends on the type of disease. Children with osteogenesis imperfecta type III demonstrate semantic learning decrease, this could be as a result of moving problems (Troitskaya, 2013).

This paper experimentally demonstrates for the first time the difference between two types of dysontogenesis. It is new important data for clinical psychologists, teachers and social care workers. For all of them, it is necessary to understand the structure of cognitive profile decline of children with different somatic diseases. This knowledge is important for clinical psychologists, teachers and social care workers for better understanding the structure of cognitive profile decline of children with different somatic diseases and the steps recommended for managing it. Additionally our work for the first time presents detailed analysis of cognitive profile of children with osteogenesis imperfecta. Unexpectedly our data revealed that not only the type of dysontogenesis itself affects the profile of cognitive decline, buteven within one type of dysontogenesis exist differences depending on the severity of the disease. We suppose that future studies should consider other types of dysontogenesis. Also, more data needs to be collected on impaired and deficient dysontogenesis.

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