

Temperament traits in 4-year-old children born prematurely – may they suggest a threat for mental functioning?

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Summary

Aim. The aim of the study was to assess emotional functioning and identification of temperamental traits in 4-year-old children born prematurely with birth weight ≤ 1500 grams. The second aim was evaluation of autism spectrum disorders frequency in this group of children.

Method. Eighty-six 4-year-old children born prematurely (gestational age ≤ 32 weeks, birth weight ≤ 1500 grams) were evaluated. All children underwent physical examination (with the assessment of motor function, vision and hearing), anthropometric measurements and psychomotor tests: Leiter International Performance Scale P-93, Children Vocabulary Test (TSD), temperament questionnaire (EAS-C), and CAST questionnaire. Parents were asked to fill in questionnaires assessing socio-economic conditions of the family and children attendance in kindergarten or early development support.

Results. In the EAS-C questionnaire hyperactivity and reduced emotionality were significantly more common comparing to population. Children with lower gestational age and lower birth weight were characterized with low emotionality score. Children with the CAST score ≥ 12 points were significantly smaller at birth, more often suffered from retinopathy of prematurity and had poorer results in neurodevelopmental tests – Leiter scale, Children Vocabulary Test.

Conclusions. Children born prematurely are at greater risk of the occurrence of hyperactivity and autism spectrum symptoms. Detection of emotional disorders in children born prematurely is essential to implement the therapeutic support as early as possible.

Key words: ASD, preterm infants, neurodevelopmental disorders

Introduction

Comprehensive care for children born prematurely continues to pose the greatest challenge for modern medicine. In first few months the main focus is on life-sustaining treatment, minimizing the negative influence of intensive care environment stress and support for parents. After discharge, the main issue is proper monitoring and comprehensive support of premature infant's development.

Prematurely born children are predisposed to variety of functioning problems later in life. They tend to present deficits in cognitive abilities and speech, higher incidence of cerebral palsy, significant visual and hearing impairments.

Severe neurodevelopmental disorders, as a consequence of central nervous system (CNS) injury, are not common. However, further development of prematurely born children can be described depending on interactions between the degree of neonatal immaturity, medical prematurity complications and neurological injuries (retinopathy of prematurity – ROP, bronchopulmonary dysplasia – BPD, intraventricular hemorrhage – IVH, periventricular leukomalacia – PVL), environmental and socio-economic factors.

Preterm birth and low birth weight (LBW) have been identified as risk factors for emotional disorders, anxiety behavior, depression, attention deficit/hyperactivity disorders (ADHD), and autism spectrum disorders (ASD) [1–5].

The focus of more recent studies has shifted to mental problems of children born prematurely, later in life. Bhutta et al. in 2002 [6] suggested that children who were born preterm have a 2.64-fold higher risk of developing ADHD (attention deficit hyperactivity disorder) at school age and frequently manifest various behavioral disorders. Johnson and Marlow proposed a “preterm behavioral phenotype” characterized by inattention and hyperactivity, social and emotional difficulties [2]. Furthermore, ex-preterms' attention problems, withdrawn behaviors and symptoms of depression are also emphasized [7]. Prominent hyperactivity and impulsive difficulties remained significant even in children born prematurely without moderate and severe disabilities [8].

The relationship between ADHD syndrome and preterm birth and very low birth weight is well documented. Recently, however, studies evaluating the prevalence of ASD (Autism Spectrum Disorder) were published [2] and results of these observations are not conclusive [9, 10].

Furthermore, recent studies results indicate that the coexistence of ADHD symptoms significantly delays the diagnosis of ASD. This information was taken into account by the authors of the new DSM-5 [11–13].

Prevalence of ASD in western populations is estimated between 0.2 and 0.7% [14, 15]. The incidence of ASD in Polish population has not yet been studied. Previously conducted analysis concerned small groups of children and was limited only to some Polish regions. It is estimated that autism is present in at least 1–2 per 1000 children [16].

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), published in May 2013 by the American Psychiatric Association [11, 13], for ASD diagnosis the existence of two core symptoms is necessary: communication and social interaction disorders as well as stereotyped, repetitive behavior. These symptoms should appear in early childhood. Diagnosis is complemented by the assessment of cognition and speech development.

Adequate and reliable screening for these disorders appears to be very important in the high-risk group of children born prematurely. Abnormalities in social interactions and communication, as well as deficits in intellectual function and speech are observed both in children born prematurely and in those with ASD [17, 18].

The focus of more recent studies has shifted to pre – and postnatal factors [4, 17, 19] which are associated with higher frequency of autism spectrum symptoms in children.

Furthermore, temperament seems to play an important role in children development, as well as in formation and manifestation of developmental disorders [20]. It was shown that temperament influences anxiety, depression and ADHD manifestation [21, 22], although there is still shortage of research trials evaluating temperamental disorders in the first years of life [23].

Recent world reports of high prevalence of emotional disorders and ASD in preterm children [17] prompted us to perform such screening in our ex-preterm population.

Aim

The aim of this study was to assess emotional functioning and temperament differentiation in 4-year-old children born prematurely with birth weight ≤ 1500 grams. Further objective of the study was the evaluation of autism spectrum disorder frequency.

Material and methods

Study population

The study included 4-year-old ex-preterms (≤ 32 weeks of gestational age, with birth weight ≤ 1500 grams). All children were hospitalized in Neonatal Pathology and Intensive Care Unit, Department of Pediatrics of Jagiellonian University in Krakow between 2008 and 2010. The study was conducted in the Follow-up Pediatric Department and Department of Applied Psychology and Human Development of the University Children's Hospital in Krakow. After obtaining informed consent from parents, all children underwent physical examination with motor, vision and hearing assessment, anthropometric measurements and psychomotor tests (Leiter International Performance Scale P-93, temperament questionnaire (EAS-C), Children Vocabulary Test (TSD) and the Childhood Autism Spectrum Test (CAST)). Parents were asked to fill in socio-demographic questionnaires assessing:

1. socio-economic conditions of the family (place of living, parents' educational status and employment, siblings);
2. children attendance in kindergarten and early developmental support.

The Ethics Committee for Clinical Investigations of Collegium Medicum, Jagiellonian University, approved the study.

Temperament questionnaire EAS-C, Buss and Plomin, Parents' version

A questionnaire to diagnose the temperament, designed for children from 3 to 7 years of age, was used in the study. The questionnaire consists of 20 items – statements, which suitability is rated by the subject on a five-point scale (from “Always true” to “Never true”). The raw results were calculated into standardized ones on the basis of population norms published by Oniszczenko and expressed on the sten scale [24]. The study assessed: Emotionality, Shyness, Sociability, and Activity.

A high Emotionality score indicates a strong tendency to easy and intense anxiety response, difficulty in maintaining calm and high sensitivity to stimuli that cause disaffection.

A high Activity score indicates a high rate of motor function (speed of action) – fast walking and speaking as well as vigor (strength and intensity of the reaction) – loud speaking, stronger hitting with toys.

A high Shyness score shows a strong tendency to respond with tension, the desire to withdraw from contacts with random people, excessive caution and fear of strangers.

Low Sociability score indicates a low motivation to look for other people and better tolerance of loneliness.

10 points on sten scale was a score considered as high (2% of the population). Low score was defined as 1 point (also 2% of population).

CAST

The Childhood Autism Spectrum Test (CAST, Polish version, 2012: E. Pisula, A. Rynkiewicz, authors of the original version: F. Scott, P. Baron-Cohen, C. Brayne [25]) for assessing the severity of autism spectrum symptoms in children was used in the study. It is designed for children aged 4 to 11 years old. Questionnaire is a 39-item (including control items), yes or no evaluation aimed at parents or child's legal guardian. Maximum score is 31 points. Scores > 15 indicate high risk of occurrence of autistic traits. Score from 12 to 15 may indicate some autism spectrum disorder presence.

Leiter International Performance Scale P-93

Leiter scale P-93 [26] is a non-verbal psychometric evaluation containing 52 subtests, organized according to the degree of difficulty. It is designed for children from 3 to 15 years of age. Besides quantitative results, it provides qualitative analysis in terms of four categories of mental operations: visual analysis and synthesis, inductive reasoning, symbols understanding and direct memory, and assessment of the cognitive style.

Children Vocabulary Test (TSD)

Children Vocabulary Test (author: Koć-Januchta M.) [27] is designed for children aged 4–7 years and measure verbal ability, both in terms of intelligibility, as well as its production. It is the only culturally appropriate vocabulary test available in Poland. As a result of the test, in addition to the overall score, two specific indicators are obtained – passive and active speech score. The Children Vocabulary Test consists of four subtests – categories, pictures, synonyms and filling gaps in sentences of the story read by the examining person. Two of them measure the passive speech and two – active speech. Testing tasks concern eight subject areas: home, food, clothing, the human body, the state, recreation, nature, feelings.

Statistical analysis

Qualitative variables were compared using χ^2 test or Fisher's exact test. Quantitative variables were compared using analysis of variance. Depending on the nature of the evaluated variables ANOVA or Kruskal-Wallis test were used. Statistical analysis was performed with the use of SPSS 23. Significance level of $\alpha = 0.05$ was assumed for all calculations. Result of the analysis was therefore considered statistically significant when p-value determined on the basis of test statistics was less than 0.05 ($p < 0.05$).

Results

Study population characteristic

Between 2008 and 2010, 103 children fulfilling inclusion criteria of our study were discharged from NICU. 89 of them agreed to participate in the follow-up study at the age of 4 (88% of available population). Three patients were not able to perform the test because of lack of cooperation. Eventually, the study group included 86 were patients. Mean birth weight of premature infants was 1034 g (SD: 278 g), and mean gestational age was 28 weeks (SD: 2.4 weeks).

Temperament questionnaire EAS-C

EAS-C test was performed in 86 out of 89 patients. High emotionality was shown in 6 (7%), hyperactivity in 21 (24%), low sociability in 4 (5%) and high shyness in 6 (7%) of prematurely born children. Results are presented in Figures 1 and 2. Distribution of the results of sociability and shyness did not differ from those predicted on the basis of population norms. Assessing the results of activity and emotionality significant differences from population norms were found. In the study group, hyperactivity and reduced emotionality were significantly more common as compared to general population. Low emotionality was found in 20 (23%) of the surveyed children.

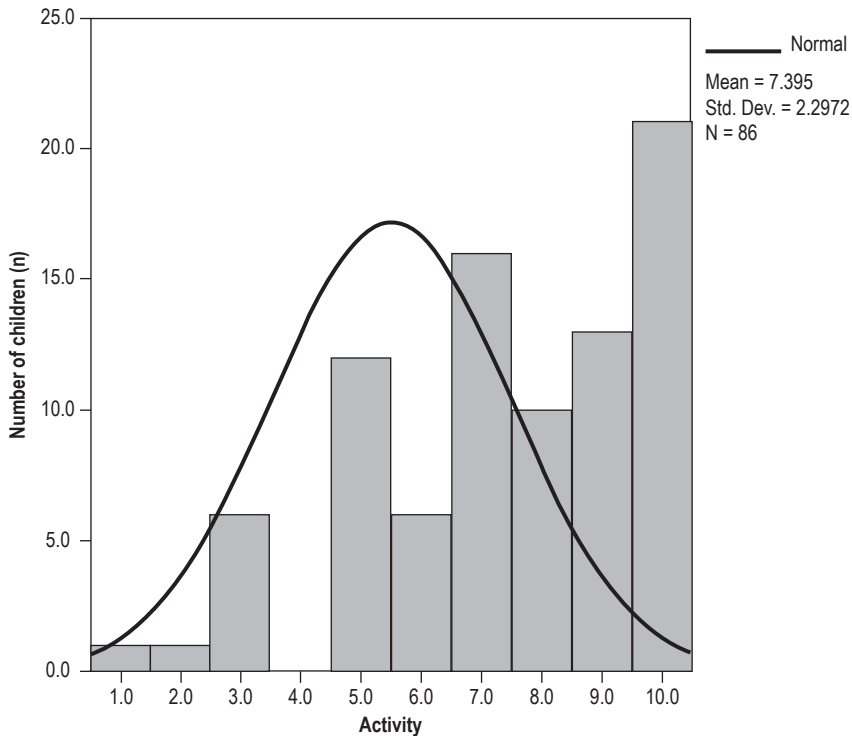


Figure 1. Activity results in study population – EAS-C questionnaire

Number of children who obtained individual activity score according to EAS-C questionnaire

Considering the results mentioned above, further analysis assesses the risk factors of:

1. hyperactivity;
2. low emotionality

Demographic and clinical characteristic of groups based on activity score is presented in Table 1. Neurodevelopmental examination results are presented in Table 2.

Table 1. Demographic and clinical characteristic of the study groups identified on the basis of activity score

	Children with an average activity (n = 65)	Children with hyperactivity (n = 21)	p
Birth weight (g) (mean; SD)	1049 (285)	973 (258)	0.28
Gestational age (weeks) (mean; SD)	27.7 (2.4)	27.9 (2.4)	0.80
APGAR 5' (Me; IQR)	6 (5–7)	6 (5–7)	0.90
Boys/girls	34/31	13/8	0.46

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IVH grade III n (%)	9 (14%)	3 (14%)	0.99
PVL n (%)	10 (15%)	2 (10%)	0.72
ROP n (%)	18 (28%)	10 (48%)	0.31
BPD n (%)	16 (25%)	5 (24%)	0.88
SGA n (%)	8 (12%)	6 (29%)	0.09

IVH – intraventricular hemorrhage; PVL – periventricular leukomalacia; ROP – retinopathy of prematurity; BPD – bronchopulmonary dysplasia; SGA – small for gestational age

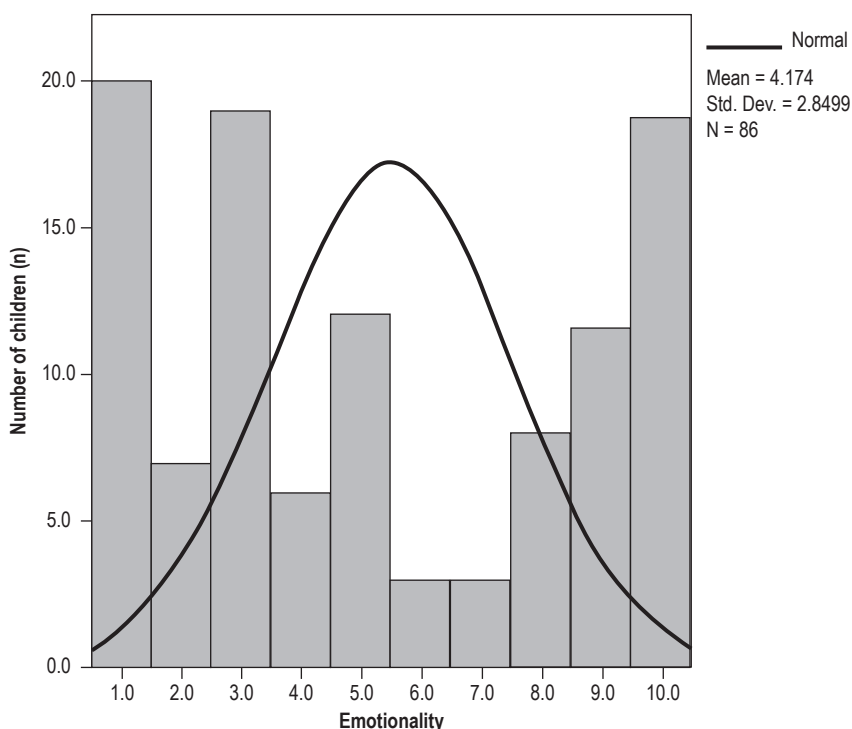


Figure 2. Emotionality results in study population – EAS-C questionnaire

Number of children who obtained individual emotionality score according to EAS-C questionnaire

Table 2. Comparison of neurodevelopmental examination results in the study groups identified on the basis of activity score

	Children with an average activity (n = 65)	Children with hyperactivity (n = 21)	p
Vision impairment/blindness	11/2	4/0	0.55
Hearing impairment	1	0	0.90

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Leiter score (mean; SD)	99 (18)	99 (18)	0.94
Decreased score in Children Vocabulary Test n (%)	27 (44)	9 (43)	1.0

There were no other significant correlations between birth parameters, early and late neonatal complications, socio-economic status of the family, child participation in rehabilitation or kindergarten, breastfeeding in infancy and the results of the activity assessment.

Demographic and clinical characteristics of groups identified on the basis of emotionality score are presented in Table 3. Neurodevelopmental examination results are illustrated in Table 4.

Table 3. Demographic and clinical characteristics of the study groups identified on the basis of emotionality score

	Children with an average emotionality (n = 66)	Children with low emotionality (n = 20)	p
Birth weight (g) (mean; SD)	1061 (270)	929 (283)	0.05
Gestational age (weeks) (mean; SD)	28.1 (2.2)	26.7 (2.9)	0.016
APGAR 5' (Me; IQR)	6 (5–7)	6 (5–7)	0.90
Boys/girls	37/29	10/10	0.79
IVH grade III n (%)	7 (11%)	5 (25%)	0.14
PVL n (%)	11 (17%)	1 (5%)	0.28
ROP n (%)	22 (33%)	6 (30%)	0.94
BPD n (%)	17 (26%)	4 (20%)	0.89
SGA n (%)	12 (18%)	2 (10%)	0.51

IVH – intraventricular hemorrhage; PVL – periventricular leukomalacia; ROP – retinopathy of prematurity; BPD – bronchopulmonary dysplasia; SGA – small for gestational age

Table 4. Comparison of neurodevelopmental examination results in the study groups identified on the basis of emotionality score

	Children with an average emotionality (n = 66)	Children with low emotionality (n = 20)	p
Vision impairment/blindness	11/2	4/0	0.58
Hearing impairment	1	0	0.90
Leiter score (mean; SD)	99 (17)	98 (20)	0.83
Decreased score in Children Vocabulary Test n (%)	28 (42.4)	8 (40)	1.00

Children with low emotionality had significantly lower gestational age and lower birth weight. There were no significant correlations between low emotionality score and early or late neonatal complications, socio-economic status of the family, child participation in rehabilitation or kindergarten and breastfeeding in infancy.

CAST

The Childhood Autism Spectrum Test was fulfilled by parents with the assistance of psychologist. Two children (2.3%) obtained score above 15 points – including one child with severe vision impairment. Three children scored between 12 and 15 points – including one with severe vision impairment and two with cerebral palsy and cognition delay.

Further analysis concentrate on additional risk factors of increased CAST score. Due to that, comparison between children with CAST results below 12 points and those with CAST result of 12 or more points was performed. Demographic and clinical characteristic of described groups is presented in Table 5. Neurodevelopmental examination results can be seen in Table 6.

Table 5. Comparison of demographic and clinical characteristics of groups identified on the basis of CAST score

	Children with CAST score < 12 (n = 81)	Children with CAST score ≥ 12 (n = 5)	p
Birth weight (g) (mean; SD)	1051 (280)	795 (215)	0.048
Gestational age (weeks) (mean; SD)	28 (2.4)	26.8 (2.5)	0.30
APGAR 5' (Me; IQR)	6 (5–7)	6 (5–7)	0.70
Boys/girls	43/38	3/2	1.00
IVH grade III n (%)	10 (12.3%)	0	1.00
PVL n (%)	10 (12.3%)	1 (20%)	0.50
ROP n (%)	22 (27%)	4 (80%)	0.028
BPD n (%)	10 (12.3%)	2 (40%)	0.14
SGA n (%)	12 (15%)	3 (60%)	0.035

Table 6. Comparison of neurodevelopmental examination results in groups created on the basis of CAST score

	Children with CAST score < 12 (n = 81)	Children with CAST score ≥ 12 (n = 5)	p
Vision impairment/blindness	17/1	1/1	0.055
Hearing impairment	0	1	0.90
Leiter score (mean; SD)	100 (17)	82 (18)	0.038
Decreased score in Children Vocabulary Test n (%)	30 (37%)	4 (80%)	0.029

It is worth highlighting, that children with CAST score ≥ 12 points were significantly smaller at birth and more often suffered from complications in the neonatal period (e.g. retinopathy of prematurity). Moreover, this group of children had significantly poorer results in neurodevelopmental tests (Leiter scale, Children Vocabulary

Test). There were no statistically significant differences in analyzed socio-economic parameters.

Correlation between CAST and EAS-C results

There is a positive correlation between CAST score and emotionality results and a negative correlation between CAST and Leiter score. The activity parameter positively correlated with sociability and negatively with shyness. Interactions between evaluated tests are shown in Table 7.

Table 7. **Interactions between EAS-C and CAST results**

	Activity	Emotionality	CAST
Activity	X	0.032 (0.38)	-0.038 (0.39)
Emotionality	0.032 (0.38)	X	0.15 (0.09)
CAST	-0.038 (0.39)	0.15 (0.09)	X
Sociability	0.36 (< 0.001)	-0.002 (0.49)	-0.065 (0.28)
Shyness	-0.18 (0.045)	0.13 (0.12)	-0.078 (0.24)
Leiter score	0.008 (0.47)	-0.05 (0.32)	-0.22 (0.023)

Discussion

Temperament is a significant factor influencing child's development. According to Buss and Plomin, it also indicates the course of individual's behavior in certain situations. It is of significant importance in interactions with environment and influences starting activities. Children choose particular situations and environmental conditions according to their potential and, among others, temperament. Temperament can both support child's development (by stimulating activity) and hinder child's functioning (by leading to non-adaptive behavior). High activity increases the multiplicity and diversity of developmental stimuli, whereas it hinders concentration and adaptation to school-type situations. High sociability positively influences social abilities, whereas high shyness causes difficulties in establishing relationships.

According to Mary K. Rothbart [21] extreme individual differences in temperament can promote pathology in the functioning, as well as temperament itself may be affected by functional disorders.

The literature is paying a great deal of attention to incidence of behavioral disorders, avoidant behavior, anxious behavior and hyperactivity. The world most popular questionnaire is Child Behavior Checklist (CBCL). However, in our study, we decided to use EAS-C questionnaire to diagnose the temperament. In the assessment of temperamental traits in the study group, it was found that distribution of sociability and shyness scores did not differ from the distribution of population-determined standards. On the other hand, hyperactivity was significantly more frequently reported compared with general population, which complies with well-documented observations of increased

frequency – up to 2–4 times [28, 29] – of ADHD in children born prematurely. Our results indicate necessity to provide further observation towards ADHD and ASD in this group later life [13, 15].

While examining risk factors of hyperactivity, we compared groups with average and increased activity. There were no notable correlations between this temperamental trait and birth parameters, prematurity complications, socio-economic status and neurodevelopmental tests results. We assume, that hyperactive children present “preterm behavioral phenotype” described by Johnson and Marlow. It is of note that we were surprised by low scores on emotionality scale which indicates a low tendency to manifest dissatisfaction, a high threshold of anxiety – generally emotional stability. Low emotionality was present in less mature children with lower birth weight.

A lot has changed in reasoning and defining autism since Leo Kanner [30] separated and described this syndrome as a congenital disorder of social development. Currently autism, according to the new DSM-5 classification, is one of the pervasive developmental disorders and affects two areas of human functioning, causing: limited ability to build social relations, difficulties in communication, and so-called “rigid patterns” of behavior, activity and interests [11, 23]. Relatively little is known about the relation between temperamental traits and autism [31]. It was found, that children who were later diagnosed with ASD, at the age of 12 months had been significantly less active, had had very strong, atypical emotional reactions and low mood [16, 20, 32, 33].

In recent years have appeared studies reporting increased frequency of autism spectrum disorders in children born prematurely. Limperoloulos and Kuban [34, 35] reported positive screening for autistic traits in 21–25% of 2-year-old children born with very low birth weight. The incidence may be overestimated due to the high frequency of developmental delay in first few years of life [36]. Prevalence of confirmed ASD diagnoses in school-aged children, according to different authors, ranges from 1–2% in children born with low and very low birth weight [37, 38] to even 26% in children in EPIBEL study [39].

Our study reveals the presence of autistic traits, measured with CAST, in 2.3% of the study group. This is slightly higher than the incidence in the general population, but not as high as reported by other authors: 22% [34], 6.4% [17], 4.5% [4]. With the tightening of diagnostic criteria and the assessment based on three tests, Stephens et al. [40] found a lower incidence – 1%. A similar incidence of ASD diagnoses was obtained by Gray et al. in one of the newest studies in children without significant neurodevelopmental disorders born with gestational age ≤ 30 weeks [10].

The causes of autism are still unknown. It is believed that both genetic [41] and external factors modifying the development of the brain and disrupting differentiation processes, synaptogenesis and myelination are important [42].

In the study by Johnson et al. [17], who investigated antecedents of ASD (diagnosed with SCQ questionnaire) among 11-year-old ex-preterms, independent risk factors were associated with child’s age. By the time of discharge from the hospital, male sex, breech delivery, abnormal cerebral ultrasound scanning results were risk factors for ASD, while breast feeding had protective function. Furthermore, male sex,

developmental disorders and aggressive behavior at the age of 2.5 years and cognitive impairment, hyperactivity, inattention and peer problems at the age of 6 years were also found as risk factors for ASD.

In the present study the occurrence of autistic traits closely correlated with low birth weight and developmental disorders: poorer results on Leiter scale and Children Vocabulary Test, as well as with vision impairments and history of ROP. These risk factors were also described by other authors [2, 17, 43].

Careful consideration should be given to interpretation of increased incidence of ASD in children with neurodevelopmental impairments. The neonatal-onset of serious vision impairment may cause symptoms similar to autism [44]. Due to the lack of visual perception sightless and partially sightless children have limited possibilities to mimic people's behavior patterns. As a result they can present limited and rigid behavior patterns, which can be misinterpreted as symptoms of autism [45]. Moreover, high CAST result may be also obtained by children with severely delayed cognitive development. It should also be emphasized that an objective assessment of cognitive abilities in this group may be hindered due to problems with communication and understanding of commands [46].

For this reason, in the assessment of cognition we used Leiter International Performance Scale because it does not require the use of verbal commands [26]. However, it should always be analyzed whether the low score obtained in the test is due to insufficient co-operation or it is the result of lack of understanding of the non-verbal commands.

Bostrom et al. [47] analyzed the temperamental traits in preschool children with autism spectrum disorders or delayed/impaired mental development. On the basis of this analysis it was found that those children could be characterized by a common pattern of temperament – with high emotionality, shyness, impulsivity, and low activity and sociability. Our study confirms the data [2, 19] about increased incidence of hyperactivity in ex-preterms, however we did not observed increased emotionality or shyness.

The American Academy of Pediatrics recommends screening of all children for ASD at 18 months. However, in children born prematurely it may not be accurate, especially when using a screening tool developed for use in general population. It seems that to decrease the rate of false positive screens caused by developmental disorders, preterm infants may require the use of screening instrument designed for a population with high rates of neurodevelopmental impairment [40]. Some researchers emphasize the validity of temperamental traits evaluation and its correlation with autistic characteristics, in order to implement early intensive intervention for ASD in patients with unfavorable emotional condition. This type of intervention positively influence further verbal, intellectual and social abilities development [16, 31, 33, 48, 49].

During CAST evaluation, we noticed remarkable difficulties in understanding and interpreting statements by parents. There was a need to analyze questions together with child's parents. Recently published studies indicate the lack of experience with a large group of children and the associated lack of a reference point to

assess their own child as the cause of parents' difficulties [50]. In our opinion, this way of conducting tests (instead of sending the questionnaire by post – used by numerous authors) would reduce the incidence of false positive results in children born prematurely. Stephens et al. [40] also highlighted that, besides test results in preterm infants, direct observation of a child and diagnosis made by psychiatrist is essential [17, 33].

Conclusions

1. Children born prematurely are at greater risk of the occurrence of hyperactivity and autism spectrum symptoms.
2. ASD screening tests filled in by parents should be interpreted very cautiously. It is recommended to analyze questionnaire statements together by a specialist and a parent, to avoid false positive screens.
3. Early detection of emotional disorders in children born prematurely is essential. The awareness of temperamental traits allows implementation of the therapeutic support when needed.

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