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Stroke in Children and Adolescents: Topical Problems of Pre-Hospital Diagnostics

Abstract

The article is devoted to the urgent problem of pediatrics and pediatric neurology: pre-hospital diagnosis of stroke in children. A review of domestic and foreign literature on the early diagnosis of stroke in children and adolescents, as well as epidemiological data on pediatric stroke, is presented. Particular attention is paid to the features of the symptoms of stroke and stroke-like conditions ("stroke masks") in the pediatric population, and the analysis of the main factors that influence errors in the early diagnosis of stroke in children and adolescents. Currently, in the diagnosis of ischemic stroke, its "masks" are found in 53.9% of cases, with hemorrhagic stroke, in 36.3%, and with transient ischemic attacks, in 9.8% of cases. One of the most common diseases that is necessary to differentiate with ischemic pediatric stroke is migraine. This problem is covered in academic writings that highlight the leading differential diagnostic criteria for migraine and stroke, and also represent a diagnostic algorithm. The clinical features of pediatric stroke, especially manifest symptoms, make it difficult to apply adult screening stroke scales in pediatrics. The article discusses the main scales for the early diagnosis of stroke in adults, and their potential application in pediatric practice. Currently accumulated experience in pre-hospital and early diagnosis of stroke in children determines the focus areas to reduce the time of diagnosis of acute cerebrovascular accidents in children, followed by the introduction of reperfusion therapy in pediatric practice.

Key words: *pediatric stroke, stroke risk scales, pre-hospital stage, emergency*

Conflict of interests

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ACVE — acute cerebrovascular event, EMC — emergency medical care, HA — headache, HS — hemorrhagic stroke, IS — ischemic stroke, VBS — vertebrobasilar system

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Introduction

Pediatric stroke is a disabling disease, which in 3-30% of cases leads to death, and 60-90% of children subsequently experience persistent neurological impairment in the form of motor and cognitive disorders, as well as neuropsychiatric disorders [1].

The first epidemiological studies of ischemic stroke (IS) in children date back to the 1970s. According to Schoenberg B. S. et al. (1978), the incidence of IS in children aged 1 month to 18 years was 0.63 cases per 100,000 children [2]. In this large-scale 10-year study, pediatric stroke was first defined as a separate issue requiring the special attention of clinicians.

Analysis of stroke incidence in children under 16 years in France for the period 1985-1993 performed by Giroud M. (1995) demonstrated a fairly high incidence of stroke — 13.02 per 100,000 children per year (95% CI 8.54-18.84), where the incidence of IS was 7.9 per 100,000 children per year (95% CI 2.56-14.57) [3].

According to the data from the Pediatric Stroke Register for the period 1992-2001 in Canada, the incidence of IS in children under the age of 18 was 1.72 per 100,000 children per year; 2.4 cases per 100,000 children per year were recorded for the same period (1993-2003) in Northern California [4, 5].

Results of the analysis of the Swiss Neuropaediatric Stroke Registry (SNPSR) for the period from January 2000 to December 2012 showed that the frequency of ischemic stroke and symptomatic cerebral sinus thrombosis in children under 16 years was 2.1 per 100,000 children per year [6].

In the later works by V. Ganesan (2011), the annual incidence rate of stroke in children over the age of one month was 0.6 per 100,000 [7]. In her work (2013), Lvova O. A. cited the following data on the incidence of stroke in children by age and country: among newborns, acute cerebrovascular event (ACVE) develops in 1 of 4,000 full-term ones, at an older age it barely reaches 0.2-0.3 per 100,000 children per year. The incidence of stroke among children under 1 year of age in the United States is 0.78 per 100,000, in France — about 1.3 per 100,000 children per year [8]. Results of the analysis on the incidence of pediatric stroke in different age groups published by Jeong G. and colleagues in 2015 amounted to 0.2-0.3 per 100,000 for children under 5 years, and 0.8-1.3 per 100,000 children per year for children aged from 5 to 14 years, which demonstrates no significant difference in comparison with previously published results [9].

Rivkin M. J. in his study (2016) reports about the incidence of pediatric stroke of 1.3 per 100,000, while for the adult population the figure is 175-200 per 100,000 [10]. In 2018, Yock-Corrales A. analyzed the accumulated information on pediatric strokes and showed that statistical data on the incidence of ACVE in children, as well as distribution by age and gender, do not differ significantly in developed and developing countries or in different climatic zones [11].

Data on the incidence of ischemic stroke in Russia are extremely scarce. In 2009, Zykov V. P. presented data on the incidence of IS in Moscow — 0.79 per 100,000 children per year [12]. According to Lvova O. A. et al. (2013), mortality in cases of IS in children ranges from 7 to 28%. For children aged under 5 years, IS mortality amounts to 15 cases per 1,000,000 annually; for children aged over 5 years — 7 deaths from cerebrovascular diseases, which is 10% of the total mortality in neurological departments. The death rate is higher among boys [8].

In more recent studies (2016-2018), there is a definite tendency for an increase in the incidence of pediatric stroke; it may be associated with better diagnostics of this pathology in the pediatric population (improved neuroimaging, concern of medical personnel about the problem of stroke in children).

Since stroke outcomes and mortality depend on timely diagnosis, the problem of early detection of ischemic and hemorrhagic brain damage in children and adolescents becomes very important. This problem was investigated in many articles, especially during the last two decades.

The objective of our work was to analyze the literature devoted to the problem of early (prehospital) diagnosis of pediatric stroke, to the features of differential diagnosis of stroke and stroke-like conditions ("stroke masks") in the pediatric population, and to analyze the use of screening scales for diagnosing stroke in children at the prehospital stage. The search for relevant scientific articles on the problem of early and pre-hospital

diagnosis of stroke in children was carried out using the pubmed.com medical scientific Internet portal. For the query with keywords "childhood stroke and stroke in children", 15,660 scientific papers were found, for the query "emergency and stroke in children" — 588 articles, "delay to diagnosis and stroke in children" — 274 articles, "differentiate in diagnostic stroke in children" — 56 articles.

The accumulated experience on the problem of stroke in children allowed specialists in different countries to formulate recommendations on the stages of providing medical care to children and adolescents with stroke: Federal Guide for Pediatric Neurology (2016, Russian Federation); The diagnosis and acute management of childhood stroke, Clinical guideline (2017, Australia); Stroke in children, clinical guideline for diagnosis, management and rehabilitation (2017, UK), and others [13-15].

The following stages of medical care for children with stroke were defined:

1) pre-hospital stage (ambulance teams, family physicians, pediatricians);
2) intensive care (centers of pediatric cerebrovascular pathology, intensive care units of pediatric departments, neurosurgical departments);
3) rehabilitation treatment (children's neurological department, rehabilitation departments and centers for children);
4) follow-up care (local pediatric neurologist, pediatrician, family physician) [16].

Children should receive high-quality qualified medical care at each stage.

Signs of pediatric stroke are to a large extent similar to those in adults: muscle weakness, impaired sensitivity and speech, facial asymmetry; but the diagnosis at the pre-hospital stage is often complicated due to the nonspecific, vague clinical pattern, which may include a variety of symptoms (headache, seizures, impaired consciousness, and others) typical for a wide range of diseases — not only of the central nervous system, but also of other organs and systems (Table 1) [17]. Other difficulties for the diagnosis of stroke in the pediatric population are associated with behavioral and age-related characteristics. For example, speech in newborns and children in their first years of life is not formed, and so they are not able to clearly define and describe their feelings. In addition, it is widely believed among practitioners that stroke is typical only for elderly patients, and IS is often not included on the list of diagnostic search performed in children for finding the possible etiological cause of present symptoms [7, 18, 19]. Many researchers have tried to describe the initial symptoms of stroke, as well as to perform a comparative analysis of the clinical manifestations of IS and hemorrhagic stroke (HS) in children (Table 1).

Table 1. *Symptoms of ischemic and hemorrhagic stroke in children according to various authors [20, 21]*

Symptoms	Earley C. J., 1998 n = 35	Mackay M. T., 2016 n = 92	Neville K., 2016 n = 53	Aroor S., 2017 n = 736	Meyer-Heim A. D., 2003 n = 35	
	IS n = 35	IS n = 55	IS n = 53	HS n = 37	IS n = 18	HS n = 17
Focal symptoms	+	+	+	-	+	+
Seizures	-	+	-	+	+	+
Cerebral symptoms	+	-	-	+	+	+
Hemiparesis	+	+	+	-	+	+
Speech impairment	+	+	+	-	+	-
Facial asymmetry	+	+	+	-	-	-
Inability to walk	+	+	+	+	+	+
Nausea, vomiting	-	-	-	+	-	+
Mental disorder	+	-	-	+	-	+
Impaired consciousness	-	-	-	+	+	+
Vision impairment	-	-	+	-	-	-
Headache	+	+	+	+	+	+

One of the main problems in pre-hospital diagnosis of stroke is the difficulty of differential diagnosis with "stroke masks" which can be found in 50-93% of all cases of primary suspicion of IS in children and adolescents [16, 21], while in adults, "stroke masks" are found in one third of patients with a sudden onset of focal neurological impairment [22].

A number of researchers analyzed the most frequent "stroke masks" that can be defined as pediatric stroke (Table 2).

Table 2. *The incidence of ACVE and "stroke masks" in pediatric population (Mackay & Yock-Corrales, 2016)*

Diagnosis	n = 102 (ACVE), n = 280 ("stroke masks")
ACVE	
Ischemic stroke	53.9%
Hemorrhagic stroke	36.3%
Transient ischemic attack	9.8%
"Stroke masks"	
Migraine	30%
Epilepsy	16.4%
Bell's palsy	10.4%
Conversion disorder	6.4%
Syncope	5%

Mackay M. T. and Yock-Corrales A. in 2016 analyzed not only "stroke masks" in children but also the frequency of different symptoms for each of them (Table 3). The authors studied case histories of 382 children with "stroke masks" and ACVEs for the period from January 2003 to December 2010. Data analysis showed no statistically significant difference between IS and HS. IS was the most common type of pediatric stroke and amounted to 55 (54%) cases; HS ranked second with 37 (36%) cases; transient ischemic attack (TIA) was found in 10 (9.8%) cases. The most frequent "stroke masks" in children with acute neurological deficit, or with symptoms of IS were the following: migraine in 84 (30%) cases, febrile or afebrile seizures in 46 (16.4%) cases, facial neuropathy (Bell's palsy) in 29 (10.4%) cases, conversion disorder in 18 (6.4%) cases, syncope in 14 (5%) cases [18, 22, 23].

In their paper, Mackay M. T. and Yock-Corrales A. defined 14 factors that increase the possibility of stroke diagnosis and 2 factors that reduce the possibility of stroke diagnosis. The sense of well-being during the week before hospitalization increased the possibility of making a final diagnosis of stroke while weakness in the arm, a neurological symptom that is considered one of the common signs of ACVE, was of low significance. Facial asymmetry

Table 3. *Symptoms of ACVE and "stroke masks" according to various authors*

Symptom	Mackay M. & Yock-Corrales A., 2016		Neville K. & Warren L., 2016	
	ACVE (n = 102)	"Stroke masks" (n = 280)	Ischemic stroke (n = 53)	"Stroke masks" (n = 53)
Headache	58/100 (58%)	161/280 (58%)	n. d.*	n. d.
Nausea, vomiting	32/100 (32%)	103/280 (37%)	n. d.	n. d.
Focal symptoms	58/102 (57%)	93/276 (34%)	35 (71%)	23 (44%)
Impaired sensitivity	17/102 (17%)	68/274 (25%)	n. d.	n. d.
Vision impairment	17/100 (17%)	66/276 (24%)	n. d.	n. d.
Seizures	21/102 (21%)	57/280 (20%)	n. d.	n. d.
Confusion	31/102 (30%)	53/278 (19%)	11 (21%)	8 (15%)
Dizziness	15/99 (15%)	58/276 (21%)	n. d.	n. d.
Speech impairment	37/102 (36%)	43/277 (16%)	9/33 (27%)	7 (17%)
Ataxia	18/101 (18%)	41/276 (15%)	n. d.	n. d.
Loss of consciousness	10/102 (10%)	35/278 (11%)	n. d.	n. d.
Disorientation	2/97 (2%)	10/274 (4%)	n. d.	n. d.
Facial asymmetry	n. d.	n. d.	21 (43%)	29 (55%)
Other symptoms	5/102 (5%)	59/279 (21%)	n. d.	n. d.

Note: *n. d. — there is no data

and inability to walk were also associated with an increased possibility of being diagnosed with stroke. In contrast, the presence of other symptoms (headache, nausea/vomiting, impaired sensitivity) was inversely related to the diagnosis of stroke. The following symptoms were also significant factors for the diagnosis of IS in the course of univariate analysis: hemiparesis, speech impairment, facial asymmetry, inability to walk. None of the children with IS had a loss of consciousness or was in coma (<9 points according to Glasgow Coma Scale). On the contrary, statistically significant factors for diagnosing a "stroke mask" included other, non-neurological (abdominal pain, dyspepsia, fever) symptoms and no neurological pathology during examination. Significant factors for the diagnosis of HS with univariate analysis were the following: sudden onset of symptoms, vomiting, borderline mental disorder, inability to walk, coma. All children with HS felt good for a week before admission, none had dizziness.

In literature, the discussion of "stroke masks" in children is often associated with the analysis of the frequency of occurrence of certain symptoms and with main directions of the diagnostic search for these signs.

Bhate S. and Ganesan V. in their work (2015) separately identified acute hemiparesis as the most common symptom of ACVE that requires differential diagnosis with a wide range of pathological conditions [24]. According to the authors, 20-30% of children with acute hemiparesis have a non-vascular diagnosis. In adults, the frequency of "stroke masks" is much lower, and acute hemiparesis is normally of vascular origin. Acute hemiparesis, except for vascular origin, can occur with underlying infection of the central nervous system (CNS), hemiplegic migraine, acute disseminated encephalomyelitis, reversible posterior leukoencephalopathy syndrome, and other conditions. Hypoglycemia in children with insulin-dependent diabetes mellitus can also be manifested by focal neurological deficit, including hemiplegia [24].

Another common symptom that requires the exclusion of pediatric stroke is seizures. In adults, seizures are more commonly related to HS; in children, the risk of their development is high in connection with both hemorrhage and ischemia. According to Fullerton H. J. et al. (2016), the seizure disorder occurs in 20-48% of cases of pediatric stroke regardless of age and type of stroke; Mackay M. T. (2018), based on his observations, reports a frequency of seizures related to IS of up to 58% [25]. The development of seizures during the first 24 hours from the onset of stroke increases the risk of epilepsy in the next 6 months [26]. Some researchers report seizures after migraine in 10% of adults, but Mackay M. T. notes that only 4% of children with migraines had seizures.

Vomiting, which is a common migraine symptom, especially in young children, is rare in connection with IS. The absence of focal neurological symptoms during examination in the emergency care department was more often associated with migraines, which is in accordance with the duration of migraine aura when focal neurological deficit usually disappears within 60 minutes, and in children often even in shorter periods of time. Therefore, an emergency medical care (EMC) physician may observe symptoms that may be a possible manifestation of ACVE but are completely resolved by the time of the patient's admission in intensive care unit [27].

Mackay M. T. [25] in his work devoted to migraine as the most frequent "stroke mask", refers to the data obtained by French researchers who examined 79,433 children with non-febrile, non-traumatic headache, which amounted to 2.6% of all calls in the emergency care department. Headache (HA) was associated with at least one neurological symptom in 102 (0.13%) cases. In the subgroup of children with HA and focal symptoms, migraine with aura was the most common diagnosis (62% of all cases); post-seizure HA related to epilepsy was diagnosed somewhat less (26% of cases). The patients were diagnosed with IS and TIA in only 6% of cases [25].

In 2016, Spalice A. et al. attempted to analyze the features of IS and migraine in children. However, their work was of rather descriptive nature with a discussion of the possible comorbidity of these diseases [27]. Other researchers, Gelfand A. A. et al. (2015), noted that migraine is not only similar to ischemic stroke in its symptoms but also increases the risk of IS development [28].

In 2018, continuing his work on diagnosing stroke and its "masks" at pre-hospital stage, Mackay M. T. emphasized the similarities and differences between IS and migraine attack (Table 4) [25]. The average

age of children included in this study was 13 years 5 months for children with migraine, and 5 years for patients with IS. All patients with ischemic stroke and one in three patients with migraine underwent neuroimaging study; 55% of patients had no neurological pathology upon admission at the hospital. Significant factors that reduce the probability of IS diagnosis were the following: older age, vomiting, impaired vision and sensitivity, cerebral symptoms and the absence of focal neurological symptoms during examination [25].

A comparative analysis of patients having migraine with aura or IS revealed that children with IS were younger (more than half of the children aged under 5 years); they had sudden onset of symptoms while migraine symptoms developed more gradually, with a predominance of vision and sensory disorders.

When discussing the results of this study, the authors emphasize that the EMC doctor plays a leading role in the diagnosis of stroke because he/she is the first to meet the patient. The correct assessment of manifest neurological symptoms has an influence on the algorithm for further diagnosis and treatment approach. Examination of patients with cerebral symptoms is always a challenge for pediatricians. According to Mackay M., the matching of the diagnosis of stroke at pre-hospital and hospital stages ranged from 51% to 81% [18].

Beslow L. A. and Lauren A. demonstrated, using the example of adult patients under the age of 50 (2017), that 21% of patients admitted at stroke departments had other, non-vascular diagnoses. At the same time, only 3% of patients aged over 50 years who were admitted at such departments with a suspected stroke were diagnosed with other diseases with clinical symptoms that are common for stroke. Speaking about the pediatric population, the authors noted that among 124 children with a referral diagnosis of "stroke", "stroke masks" were diagnosed in 76% of cases, which greatly complicates the work of EMC specialists [16].

Challenges facing EMC physicians lie in the differential diagnostics of different stroke-like conditions in children, which is necessary for the routing of patients' data to centers where round-the-clock radiation diagnostics can be performed, and, if necessary, emergency reperfusion therapy with consideration to a "therapeutic window". Screening scales can be an effective tool for early diagnostics of stroke in such cases.

Table 4. *Symptoms of ischemic stroke and migraine (Mackay M. T., 2018)*

Symptom	Ischemic stroke (n = 55)	Migraine (n = 84)
Acute onset	46 (84%)	54/83 (65%)
Headache	26/53 (49%)	83/83 (100%)
Nausea, vomiting	9/53 (17%)	39/83 (47%)
Limb weakness	40 (73%)	23/83 (28%)
Impaired sensitivity	9 (16%)	37/83 (45%)
Vision impairment	8/53 (15%)	35/82 (43%)
Seizures	12 (22%)	3/83 (4%)
Mental disorder	11 (20%)	11/83 (13%)
Dizziness	7/52 (13%)	19/83 (23%)
Speech impairment	28 (51%)	21/83 (25%)
Ataxia	13/54 (24%)	5/82 (6%)
Impaired consciousness	0 (0%)	4/83 (5%)

Early (pre-hospital) stroke scales

For the purpose of early detection of conditions suspected of ACVE at the pre-hospital stage, as well as for the purpose of differential diagnostics of ACVE and "stroke masks", special pre-hospital (or emergency, urgent, resuscitation) stroke scales are used. Currently, the most famous scales for pre-hospital diagnostics of stroke are FAST with BE-FAST modification, COTS, CPSS, ROSIER, and LAPS.

FAST — face, arm, speech, time. This scale was developed in the UK in 1998. The patient is asked to smile or to show teeth to assess facial symmetry; raise both hands up to an angle of 90° to assess muscle strength, or hemiparesis; the patient is asked to say a simple phrase to exclude speech impairment. If one of the above symptoms is found, the patient should be immediately hospitalized in a specialized hospital, which is relevant to the fourth element of the scale — time.

BE-FAST — balance, eyes, face, arm, speech, time — a modification of the FAST scale, which complements FAST with the assessment of coordination and vision impairments. FAST and BE-FAST scales were designed for use by paramedics for suspected stroke.

COTS (Central Ohio Trauma System) — includes 4 symptoms: decreased level (disorder) of consciousness, slurred speech, facial asymmetry and unilateral absence of active movements in extremities. Each item is rated as 0 (no signs), or 1 (signs are present), and so the total score ranges from 0 (no symptoms) to 4 (all symptoms). This scale is recommended for EMC specialists.

CPSS (Cincinnati Prehospital Stroke Scale) — Cincinnati scale — a scale for pre-hospital diagnostics of stroke including three positions: facial asymmetry, weakness in arm, speech impairment. Finding deviations in any of these items indicates the presence of a stroke in the patient with high sensitivity (66%) and specificity (87%) [18].

ROSIER (Recognition of stroke in the Emergency Room) — a scale for the early diagnostics of stroke in emergency care departments, in emergency rooms, or in intensive care units. In some countries, it is used by EMC physicians. According to this scale, the following symptoms are defined: impaired consciousness, seizures, asymmetric weakness of upper extremities, asymmetric weakness of lower extremities, facial asymmetry, speech impairment, vision impairment. Each symptom has its own score; the first two symptoms (impaired consciousness and seizures) have a score of "-1" as unlikely symptoms for stroke; other symptoms have a score of "+1" being typical for stroke. With a total of 1 or more points in the course of assessing patient's status, the physician suspects a stroke.

LAPS (Los Angeles Pre-hospital Stroke Screen) — a stroke scale for EMC based on the same criteria as the above scales: facial asymmetry, weakness in arm, speech impairment — but it also includes some additional items: age — more than 45 years, blood glucose, history/no history of seizures.

These scales are the main tool for EMC physicians in the quick differential diagnostics of stroke and stroke-like conditions ("masks"); they help to reduce the time between the onset of the first symptoms of stroke, hospitalization and neuroimaging confirming a stroke.

The above scales were developed and are successfully used in the pre-hospital diagnosis of stroke in adults but their use in pediatric practice has shown their low informative value [26, 29, 30].

In 2015, Bhate S. and Ganesan V. describing the differential diagnostics of acute hemiparesis in children in their work discussed the effectiveness of using the FAST scale in children. This scale can be used in older children but in younger ones, motor impairment may be less pronounced, and speech assessment is difficult [24]. In 2017, other researchers — Aroor S., Singh R. and Goldstein L. B. — compared the FAST scale with its BE-FAST modification [29]. Of the total of 736 patients included in this study, 104 (14.1%) patients had no FAST symptoms at the time of the examination. In most patients without FAST symptoms, gait disturbance (33%), decreased muscle strength in legs (10%), vision impairment (40%), and other non-FAST symptoms (8%) were observed. The use of the BE-FAST scale reduced the number of "undiagnosed" strokes from 14.1% to 4.4%, and it was also shown that patients for whom the BE-FAST scale was informative were younger and had more significant neurological deficit (according to Ped-NIHSS — Pediatric National Institutes of Health Stroke Scale — a scale for defining the severity of pediatric strokes) [30]. In addition, the authors, in the course of analyzing the data of magnetic resonance imaging (MRI) in the studied cohort of patients, found that 71% of strokes missed while using the FAST scale were limited to the vertebral-basilar arterial system; this fact was also mentioned by Beslow L. A. (2017) and Mármol-Szombathy I. (2018) [16, 31]. The proportion of missed strokes in the vertebrobasilar system (VBS) was reduced to 43% when using the BE-FAST scale.

Despite the fact that the BE-FAST scale is more effective for verification of pediatric stroke than the FAST scale, it disregards cerebral symptoms, decreased level of consciousness and seizures, which are typical for strokes in children.

When comparing the informative value of stroke diagnostic scales, Mackay M. and Churilov L. (2016) used CPSS and ROSIER scales. The authors conclude that adult stroke detection tools do not work well for the pediatric population and need to be modified because the use of CPSS and ROSIER scales by EMC physicians does not allow to accurately distinguish a stroke from its "masks" [18].

Another attempt to analyze the diagnostic value of pre-hospital scales was made in 2016 by Neville K., who retrospectively investigated sensitivity/error and features of stroke diagnostic scales, including cases with seizures as the first symptom of stroke. The author included in this analysis all children aged under 19 years who had a medical history of acute clinical symptoms and IS confirmed by MRI. The control group included patients with focal neurological symptoms brought to the emergency care department. Assessment according to COTS scale was performed, which was derived from CPSS and LAPS scales. The COTS score was calculated on the basis of neurological examination in the first record made by a neurologist, and for patients from the control group — in the first record made by a pediatrician. The median COTS score was 1.0 for both groups. However, the author concludes that despite the higher COTS score in children with stroke, these differences were statistically insignificant and using this scale in pediatrics does not improve the differential diagnostics of stroke with its "masks". Several elements — such as unilateral weakness of arm — can be used to develop a scale for pediatric strokes but it also requires some other parameters [32].

FAST, COTS and ROSIER scales in children were tested by Gorman K. M. and Wainwright M. S. (2017). The authors reported that in 54% of children who were assessed using these scales, different "stroke masks" were diagnosed. One of the important symptoms of stroke is speech impairment but there can be difficulties in its assessment in children. In said study, a full assessment using the scales (including speech assessment) was possible only in 61% of patients. Based on the results of this work, researchers concluded that these scales were less informative in pediatrics than in adult practice; this fact confirmed the need for the development of specific screening scales for diagnosing stroke in children, which will include the assessment of seizures [33].

Currently, due to vague clinical findings, the large number of "stroke masks", the lack of specific scales for pre-hospital diagnostics of stroke in children, both in developing and economically developed countries, there is a problem of delayed provision of pre-hospital care for children with suspected stroke and delayed hospitalization in a specialized hospital. There are only few publications in specialized literature on the timing of hospitalization and diagnosis from the onset of stroke symptoms in children. According to Rafay M. (2009), the average interval from the onset of symptoms to diagnosis is 22.7 hours (7.1-57.7 hours) [34]. It takes an EMC team an average of 1.7 hours (from 49 minutes to 8.1 hours) to deliver a patient to the hospital. Stojanovski B. et al. (2017) note that the immediate call for emergency medical care is a key factor in reducing the time of hospitalization for a stroke [35]. The authors point to limited public awareness of pediatric stroke (insufficiently clear description of symptoms when parents call an EMC operator) and the non-specificity of primary symptoms in children. Low diagnostic sensitivity (matching the diagnosis made by EMC specialist and the final diagnosis made in hospital) can be caused by the fact that the probability of stroke in children is not considered in the guidelines for paramedical clinical practice. In the study, only 68% of children with a referral diagnosis of ACVE were admitted to stroke centers [35]. The problem of delayed hospitalization and diagnosis in children with symptoms of stroke requires further study.

In 2014, when analyzing medical records of 287 children, Mackay M. noted that 21 of them were diagnosed with IS (7% of hospital admissions), while among 20 children who were suspected of having a stroke, the diagnosis was confirmed in 13 (65%) cases [36]. The sensitivity of stroke diagnostics among EMC physicians in this study was 62%. When comparing the sensitivity of emergency stroke diagnosis in children at the Australian Center (62%) with similar data in adults, it was found that in the latter it reaches 90% [35]. The biggest challenges in the diagnostics of ACVE are in younger children and when a stroke is localized in the vertebrobasilar system [36]. With this localization, the first symptoms of stroke may be dizziness and vomiting rather than focal neurological symptoms; this fact also complicates diagnostics at pre-hospital stage [32].

Thus, the analysis of literature data on pediatric stroke revealed that the main factors causing delay in its diagnosis in children at the pre-hospital stage are: underestimation of the severity of the child's condition by parents and guardians, and, as a result, late seeking of medical help; exclusion of the

Table 5. *Factors of the late diagnosis of stroke in children at the pre-hospital stage*

Modifiable factors	Unmodifiable factors
Delay in seeking medical advice	Features of the onset of stroke in children and adolescents
Lack of clinical suspicion in EMC doctors regarding pediatric stroke	Variety of "stroke masks" in children
Lack of valid screening scales for early diagnosis of pediatric stroke	

possibility of a child having a stroke by the EMC physician, EMC technician, paramedic; non-specific symptoms of a pediatric stroke with a large number of "stroke masks"; lack of proper screening scales for the early diagnostics of stroke in pediatrics. In order to determine the main directions in improving the quality of pre-hospital diagnostics of stroke in the pediatric population, all these factors can be divided into modifiable (factors that may be influenced) and unmodifiable factors (Table 5).

Conclusion

The increase in the number of diagnosed strokes in children and adolescents around the world makes the problem of early diagnosis and timely treatment relevant. In many countries, there were studies on the pre-hospital diagnosis of stroke in pediatrics, and, despite different healthcare systems and different organization of the emergency medical care, the same problems were defined for the early detection of stroke in children. According to foreign literature, the time interval from the symptoms onset to hospitalization in a specialized department is longer for children with stroke than for the adults; it averages 22 hours. This fact determines the need for work in this area, taking into account the large number of confirmed strokes in pediatric population. It is especially worth noting that the work of specialists in pediatric stroke should be carried out in several areas, including educational activities to inform pediatricians and parents about the problem of pediatric stroke; training activities — for physicians and EMC doctors about the signs of stroke and "stroke masks" in children; scientific activities — on the design and development of pre-hospital stroke scales in pediatrics.

Author Contribution:

I. O. Shchederkina, A. M. Sidorov, V. A. Kadyshev: concept and design of the research

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