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Features of neurohumoral regulation in flat back posture and initial stage scoliosis

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ABSTRACT

Introduction: The appearance and progression of idiopathic scoliosis (IS) are considered to be the result of an inequality of the spinal column and spinal cord longitudinal growths. Consequently, normal afferent input from spinal cord elements to the highest parts of the central nervous system (CNS) is altered even by a minor hyperextension of spinal cord structures. De-afferentiation leads to forming a hyperactive deterministic structure and inadequacy of neurohumoral processes of regulation in thalamus–hypothalamus–hypophysis. The resulting neurohumoral abnormalities could be defined in experimental models via patients' blood serum testings.

Aim: The aim of this study was to define prognostically valuable biotest indexes in the early stages of scoliotic deformity progression.

Materials and methods: Results of blood serum testing of 15 children with flat back posture and 15 children with first and second grade IS, subjects 9–12 year old, are presented in this paper. Biotest results of 12 healthy children of the same age served as the control. Method of biotesting: rats spinalized at the thoracic level (Wistar male rats weighing 200 g) were injected with 0.1 mL of blood serum of investigated children at the L3–L5 levels. Features of the rearrangement at the spinal cord level were judged by changes in the spontaneous and evoked electromyographic (EMG) activity of the hind extremities. The EMG rate is the quantity of EMG discharges in a time unit. Initial EMG activity of a rat before blood serum administration is considered to be 100%. The total coefficient of disorders was calculated according to 24 factors of antagonistic muscles EMG reactions. All patients were examined employing the following methods: computer evaluation of surface topography, surface EMG of paravertebral muscles, four-field weighting, and blood samples for biotesting.

Results and discussion: The most informative biotest indexes pointing to IS progression in children were chosen. Reliable differences in the groups with respect to the model were identified by tonic reaction changes and irradiation of excitation to muscles of an opposite extremity after electrical stimulation ($p \leq 0.05$). Reflex responses in IS were changed on one of the sides (right in right-sided and left in left-sided scoliosis), but in postural fault EMG activity increased in extensors on both sides.

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Conclusions: Biotesting findings allow for the progression of scoliotic deformity to be prognosticated. This is important for the selection of the proper treatment strategy.

1. Introduction

Unilateral trauma of the spinal cord is experimentally proved to underlie postural asymmetry.[4,21] Posttraumatic postural fixation occurs in definite time[5] and is caused by bioactive peptides called factors of postural asymmetry (FPA).[17] FPA enter cerebrospinal fluid from the hypophysis (in particular neurohypophysis), where they are synthesized and accumulated, and are transported to the target cells in spinal cord centers which regulate muscle tone.[18] Research studies concerning FPA appeared to be the basis for investigating neurohumoral regulation mechanisms in motor pathologies of diversified genesis. The presence of FPA in rats' blood serum, neurolymph and brain extracts was experimentally revealed.[1,3]

The most probable mechanism of FPA biosynthesis is similar to neurohormones production by hypothalamo-neurohypophyseal complex (HNC) which entails protohormones synthesis in paraventricular and supraoptical nuclei of hypothalamus, from where they are transported into neurohypophysis via axons of the neurons of these nuclei. Thus, unilateral brain trauma or dysfunction initiates the process of FPA activation in the hypophysis.

The revealed FPA are thermoresistant, have 1 kDa molecular weight, and can be inactivated with proteolytic enzymes. These characteristics point to their oligopeptide origin.[16,17]

High-performance liquid chromatography has helped to reveal that right- and left-sided FPA are multicomponent. Each of them consists of several (admittedly five) oligopeptides, determining their unilateral activity in a biotest.[19,18] Differences of right- and left-sided FPA not only in biological features but physical and chemical characteristics allowed for formulating the thesis of chemical differences in symmetrical zones of the central nervous system (CNS).[10,17]

The structure of one of the FPA was decoded. It was revealed to be a peptide similar in its amino acid structure to arginine-8-vasopressin (AVP).[18] Synthetic AVP administered experimentally in a dose of 10^{-14} mg causes right-sided postural asymmetry like FPA produced by animal donors. Malfunction alarm is supposed to be a substance or substances of trophogenic origin that transfer information concerning disruption with axonal current. Moreover, FPA were shown to be produced in CNS structures which lack adequate afferent input.[3] The resulting chemical asymmetry is an inductive phase of functional asymmetry of spinal centers. Thus, basic bioelectrical patterns of donor asymmetry–selective bioelectric activity increase in contralateral flexors and ipsilateral extensors with a predominance of flexor component are reproduced. Thus, bioactive substances of peptide origin are involved in the process of realization of any, including pathological, alteration of neural system activity in structural and functional deviations or brain activity failure of any etiology.

One of the FPA characteristics, its species-nonspecificity,[1,2] allows for the activity of human FPA to be biotested in animals. Based on this, it was possible to develop diagnostic methods for a preclinical discovery of movement disorders of any etiology.[1,2]

We previously supposed that during this process, the discharging of regulatory substances of peptide origin as analogs of FPA to blood was possible.[6,7]

Flat back type of postural fault also depends on the inequality of the spinal column and spinal cord longitudinal growths; as a consequence, the flattening of physiological spine curvatures occurs, primarily lumbar lordosis and a decrease in pelvic tilt. This type of postural fault leads to a decrease in the buffering function of the spine. Thoracic and abdominal muscles are weakened in flat back children. This is also one of the trigger mechanisms of frontal spine deviations and torsion of vertebral body columns around the spinal cord.[8]

2. Aim

The aim of this study is to define prognostically valuable biotest indexes in the early stages of scoliotic deformity progression.

3. Materials and methods

Results of blood serum testing concerning 42 children (11 boys and 31 girls), aged 9–12 years, undergoing treatment in the State Institution of Health Service Saint Petersburg Rehabilitative Centre of Pediatric Trauma and Orthopaedics "Ogonyok" (Saint Petersburg, Russia) are presented in this paper. Among the studied subjects, 15 children had flat back and 15 had first and second grade idiopathic scoliosis (IS) (5–20° Cobb angle). Biotest results of 12 healthy children of the same age served as the control: control group – children without infectious diseases, with spinal axis according to the physiological rate in three dimensions; IS group – children with physiological spine curvatures flattening with frontal deviation and rotational component; postural fault group – children with physiological spine curvatures flattening with potential frontal deviation without rotational component.

Clinical examinations of children with IS and flat back revealed muscle weakening, insignificant vertical asymmetry of shoulder girdles and lower angles of scapulas, winged scapulas, waist triangles **(triangle** between body and arm**)** asymmetry, and physiological spine curvature flattening (primarily lumbar lordosis flattening).

Investigations were performed on the Wistar line male rats ($n=50$) weighing 200 g. Animals were held in standard vivarium conditions with natural lighting and free water

and food access in accordance with the rules of the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes (Strasburg, 1986).

3.1. *Clinical methods of examination*

All patients were examined employing the following methods: clinical observation, computer evaluation of surface topography; computer optical topographer with TOPD software was used for surface optical topography (Certificate RU.АЯ79.B11339; METOS Medical Topographical Systems, Novosibirsk, Russia).

Significant lateral difference of the spine line in the frontal plane is considered to be 9° and more. Significant rotational difference for the thoracic spine is considered to be more than 5° and for the lumbar spine more than 3° (according to the technical documentation). Moreover, surface electromyography (EMG) of paravertebral muscles, four-field weighting, and blood samples for biotesting were taken.

3.2. *Method of biotesting*

Rats spinalized at the thoracic level were injected with 0.1 mL of blood serum of investigated children at the L3–L5 levels (1 child=1 rat; control – 13, flat back – 18, IS – 19). The rates of spontaneous and evoked EMG reactions of tibialis anterior muscle and gastrocnemius muscle of both hind extremities were recorded before, 20 min and 40 min after the injection. The EMG rate is the quantity of EMG discharges in a time unit. The initial EMG activity of a rat before blood serum administration is taken as 100%. EMG reactions were evoked with an electrical stimulus of 1 kHz and 1 mA, grouped in 3–5 bouts with 30 ms intervals. Findings were compared with the initial data with respect to 24 factors of EMG responses: rising (no less than 30%) or depression (no less than 50%) of spontaneous or evoked EMG, abnormality of reciprocalness in the evoked response of antagonistic muscles of an extremity, irradiation of excitation to muscles of an opposite extremity, multidirectional spontaneous and evoked EMG responses. A degree of abnormality manifestation is valued in points. Spontaneous EMG: 0 points – change less than 30%, 1 point – change of 30–49%, 2 points – change of 50–80%, 3 points – change more than 80%. Evoked EMG: 0 points – change less than 50%, 1 point – change of 50–70%, 2 points – change of 70–100%, 3 points – change more than 100%. Abnormality of reciprocalness: 0 points – the same as before blood serum injection, 1 point – no more than 50%, 2 points – more than 50%. Irradiation of excitation to the muscles of the opposite extremity: 0 points–irradiation is absent, 1 point – to the same muscle of the opposite side, 2 points – to both muscles of the opposite side. Multidirectional abnormalities of spontaneous and evoked EMG – 1 point. Asymmetry of abnormalities (on the right, on the left) – 1 point.

The sum is the coefficient of movement disorders. Asymmetry coefficient, pointing at right- or left-sided preferential abnormalities, was also calculated (separately counted points, reflecting the changes of EMG responses in the muscles of the right and left extremities). The total coefficient exceeding 3–5 points indicates abnormalities in the donor's motor system.

3.3. *Statistical method of experimental data analysis*

Statistical correlations of two samplings were evaluated with nonparametric Mann–Whitney U test (Statistica 6.0) with a significance level of $p \leq 0.05$.

4. Results

4.1. *Clinical evaluation*

All children were examined at the State Institution of Health Service Saint Petersburg Rehabilitative Centre of Pediatric Trauma and Orthopaedics "Ogonyok." Clinical examinations of children with IS and flat back revealed muscle weakening, insignificant vertical asymmetry of shoulder girdles and lower angles of scapulas, winged scapulas, waist triangles asymmetry, physiological spine curvature flattening (primarily lumbar lordosis flattening).

Instrumental examinations:

- *Computer optical topography*: frontal deviation did not exceed 10° in postural fault and 16° in IS, but rotation was more evident in IS.
- *Surface EMG* of paravertebral muscles revealed no significant differences.
- *Four-field weighting*: varied foot-bearing more often occurred in first and second grade IS.
- *Radiograms* were taken before hospitalization at local outpatient clinics.

Fig. 1 shows diagrams of children's tests at the early stages of scoliotic deformation development. Blood serum of a healthy child does not evoke significant changes in the motor system of a recipient rat (features of spontaneous EMG and reflex responses of the muscles). Blood serum of children with first grade IS (more than 10° Cobb angle) and flat back demonstrates significant changes of reflex EMG reactions of a recipient. Asymmetry reactions are generally seen in IS, but blood serum of flat back children evokes, as a rule, a symmetrical increase of EMG rate in extensor muscles (tibialis anterior muscle).

Fig. 2 presents biotest mean value analysis in two groups. We chose the most informative indexes of IS progression in children.[6,7]

Reliable differences in the groups were identified by tonic reaction changes and irradiation of excitation to muscles of an opposite extremity after electrical stimulation of tibialis anterior and gastrocnemius muscles. The mean value of the coefficient of movement disorders was 10.7 ± 1.2, indicating no difference between both groups. Tonic reactions in IS were 4-fold higher than in postural fault. Reflex responses in IS were changed on one of the sides (right in right-sided and left in left-sided IS), but in postural fault they were higher in extensors. Irradiation of excitation to muscles of an opposite extremity in IS was twice as much as in postural fault.

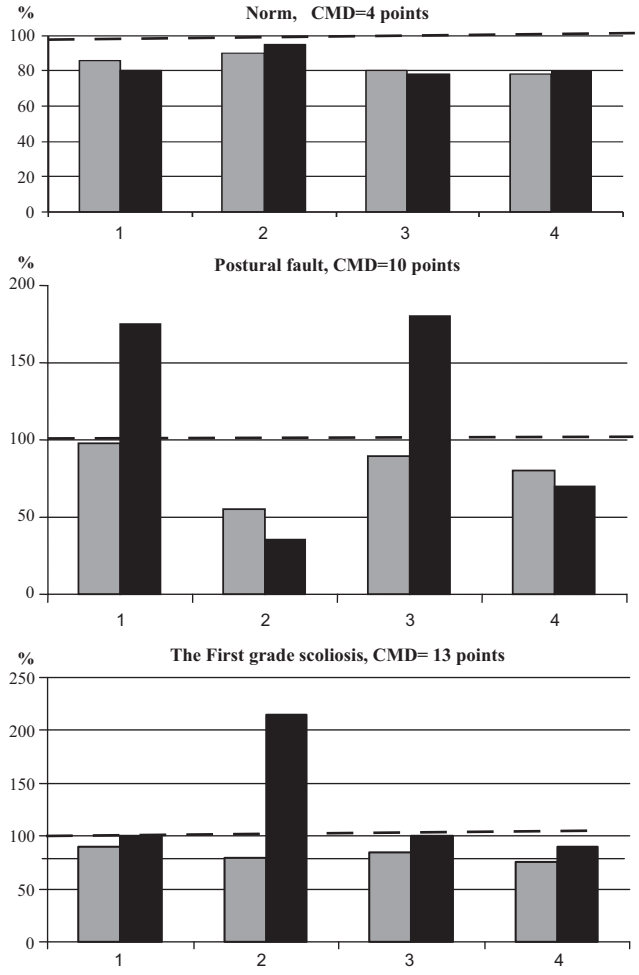

Fig. 1 – Definitive examples of changes in spontaneous and evoked EMG rates in rats in response to children's (9–11 year old) blood serum injection. Comments: *the abscissa*: 1, 3 – tibialis anterior muscle, 2, 4 – gastrocnemius muscle on the right and left side, respectively; CMD – total coefficient of movement disorders; *the ordinate*: spontaneous (gray columns) and evoked (black columns) rates of EMG discharges in 5 s analysis in percents. The dotted line – level of rat's EMG activity before serum administration.

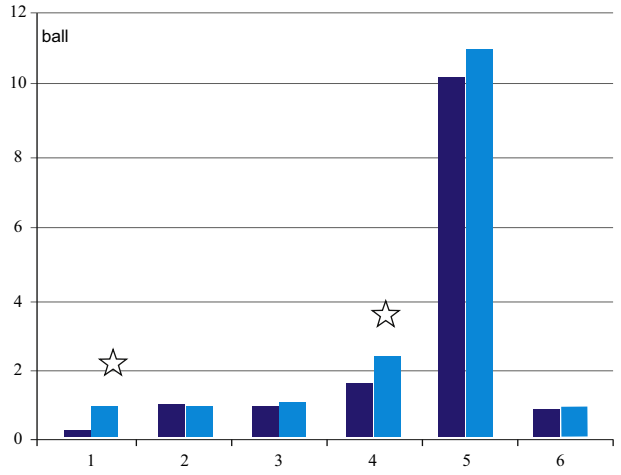

Fig. 2 – Biotest mean values of children with postural fault and initial stage IS. Comments: black columns – flat back children ($n=15$); white columns – first and second grade IS ($n=15$); *the abscissa*: 1 – tone, 2 – reflexes, 3 – reciprocalness, 4 – irradiation of excitation, 5 – coefficient of movement abnormalities, 6 – EMG reactions asymmetry on the right and on the left; *the ordinate*: evaluation in points between the groups $p \leq 0.05$.

5. Discussion

The appearance and progression of IS are considered to be the result of an inequality of spinal column and spinal cord longitudinal growths. Inadequacy of neurohumoral processes of regulation in thalamus–hypothalamus–hypophysis leads to the inequality of anatomical proportions.[7] Consequently, normal afferent input from spinal cord elements to the highest parts of the CNS is altered even by a minor hyperextension of spinal cord structures. De-afferentiation, as already mentioned,[3] leads to forming a hyperactive deterministic structure[8,13] and is supported by vicarious reactions. These reactions are directed both to growth suppression because of a decrease in osteotropic hormones profile stimulating bone formation and to spinal column torsion resulting from asymmetric tonic forces distribution of spine movement providing muscles.[15] A clinical development of IS is associated primarily with a long-lasting, uncontrolled, asymmetric distribution of paravertebral muscle tone. Progression of IS[6] and treatment effectiveness[9,12,20] could be prognosticated by biotesting.[11] Most of the flat back children subsequently develop a scoliotic deformity. Frontal spine deviation is difficult for visual evaluation both in flat back and in initial grade IS. Nevertheless, Adams's test showed no paravertebral asymmetry in flat back children unlike in children with IS.

We attempted to find objective markers of a possible deformity progression by means of children's blood serum biotesting. Clinical and experimental investigations were necessary for this purpose. Prognosis was supposed to be positive if the coefficient of movement disorders was not higher than 7–8 points.[6] Testing of children revealed the coefficient of movement disorders in healthy children to be no more than 4 points and in flat back children no more than 9 points. Repeated examinations of children (in 1.0–1.5 years) demonstrated that if the coefficient of movement disorders was initially higher than 9 points, progression of spinal deformity which subsequently led to IS had been revealed.

6. Conclusions

Biotesting of children's blood serum in the early stages of IS allowed for specifying the most informative factors of deformation development in children. Significant differences in the groups (flat back and IS) were revealed with respect to tonic reaction changes and irradiation of excitation on electrostimulation to the muscles of the opposite side ($p \leq 0.05$).

Reflex responses in IS changed on one of the sides (right in right-sided IS and left in left-sided one). In flat back, EMG

activity increased in the extensor muscles on both sides. These findings also allow for predicting the process to be progressive or non-progressive. This is important for the selection of further strategy concerning the patient's management.

Conflict of interest

None declared.

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