Optimization of orthodontic treatment for children with Angle class III malocclusion by determining the influence of blink-reflex indices

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Abstract

Background: The actual problem is developing the neurophysiological criteria for the diagnosis and monitoring of children with Angle class III malocclusion, because in this pathology there is a wide range of preclinical disorders with adverse influences upon various functions of the body. The interdisciplinary approach is supplemented by neurophysiological diagnosis, which facilitates a correct monitoring of orthodontic treatment during the mixed dentition stage. In recent years, neurophysiological methods gained a wider spread in the diagnosis and monitoring of children with Angle class III malocclusion. Aim of the study: assessing the correlations between the blink reflex indices and the degree of anxiety or anticipated pain.

Material and methods: Fifty eight children aged from 9-12 years, who were divided into 2 groups, statistically equivalent by age, gender, facial development degree, presence of a balanced psycho-emotional state. Patients in both groups were examined using traditional clinical exams and complementary exams were completed through neuro-physiological examination of the blink reflex. In our studies, we performed a correlative analysis between the R3 indices (presence/absence), the degree of dental anxiety, assessed on the Dental Anxiety Scale according to N. Corah and pain self-assessment indices based on the Visual Analogue Scale (VAS).

Results: In children with Angle class III malocclusion, in the blink reflex complex, in 31% of cases the R3 wave is present, which is associated with psycho-emotional mechanisms of inhibition/activation for anticipated pain.

Conclusions: Perspective future research in children with Angle class III malocclusion needs to be focused on uncovering the correlation between the expression degrees of trigeminal reflexes with the functional disorders in the stomatognathic and extra-stomatognathic systems (vestibular functions, pain syndromes, etc.)

Key words: malocclusion, blink reflex, interdisciplinary approach.

Introduction

The diverse ethiopatogenesis of Angle class III malocclusion requires an interdisciplinary approach in the diagnosis and treatment of this orthodontic disorder. From recent scientific sources, it can be observed that the interdisciplinary approach is supplemented by neurophysiological diagnosis, which facilitates a correct monitoring of orthodontic treatment during the mixed dentition stage. In recent years, neurophysiological methods gained a wider spread in the diagnosis and monitoring of children with Angle class III malocclusion. It has been demonstrated that many of the clinical manifestations of this pathology are associated with the activity of the trigeminal system [15], but it is still unknown how the activity of this system changes in accordance with disease severity, applied therapeutic methods, etc. Currently, research is being conducted on trigeminal reflexes in order to individualize the orthodontic treatment [13]. This aspect of the problem is perspective because clinical manifestations in children with Angle class III malocclusion (orthodontic pain, disadaptive functional disorders in the muscle activity, etc.) are associated with the trigeminal system activity [6]. It is essential to develop comprehensive diagnostic methods (clinical and neurophysiological), due to the fact that an efficient orthodontic treatment of Angle class III malocclusion will not be limited only to the clinical manifestations at the occlusion level. Therefore, as a working hypothesis for this study, we conceived that the realization of a complex diagnosis in children with Angle Class III malocclusion, by associating orthodontic and neurophysiological methods may lead to an increased efficiency of occlusal rehabilitation, by individualizing the effect on the stomatognathic system.

Aim of the study: assessing the correlations between the blink reflex indices and the degree of anxiety or anticipated pain.

In order to accomplish the proposed objectives there were applied modern scientific methods of neurophysiological research with corresponding statistical processing. There were applied neurophysiological investigation methods of the brainstem structures, trigeminal reflexes and of the muscle adaptive potential for the stomatognathic system muscles [11].

Specific for the orthodontic pathology is that it creates different pathogenic conditions for the initiation of muscle dysfunction; tooth movement during orthodontic treatment process is causing not only pain, but also significant changes in the muscles of the stomatognathic system. Different variations of occlusal pathology are associated with specific changes not only in the muscles of the stomatognathic system, but also in different muscle groups at distant sites (muscles of the neck, trunk, arms and legs) [2,8].

The start of neuromuscular era in orthodontics is based on extending the knowledge about the interaction of the trigeminal somatosensory afferentation with the cerebral structures involved in the motor activities, including the stomatognathic system (chewing, etc.) [15].

It has been shown that there are two trigeminal nerve areas of greater importance in the brainstem area for the afferentation of oral and temporomandibular joint areas: the first area is situated between Vi/Vc (*nucleus interpolaris* and *nucleus caudalis*); the second one, Vc/$C_{1,2}$ – between *nucleus caudalis* and upper cervical dorsal horns [3,4]. It was assumed that these areas have different functional roles in the painful and inflammatory phenomena, associated with the trigeminal nerve and the oromaxillofacial area. In experiments on animals, it has been shown that during temporomandibular joint inflammation, the neurons from $Vc/C_{1,2}$ activate, subsequently the impulses ascend with a modulatory effect on the intermediate zone of Vi/Vc [17]. In other experiments, it was also demonstrated that morphine injection in the Vc/C_1 area has altered the evoked potentials by 30% from the Vi/Vc area [14]. Important for orthodontics is that the nociceptive afferentation in the oromaxillofacial area, activates mainly the Vi/Vc area.

Trigeminal system is quite complex in its structure and function. This system is involved in the pathogenesis of various diseases (dental, neurological, neurosurgical, vertebroneurological, etc.). In each of these domains, different aspects of the system are being studied. One of the trigeminal reflexes that has a wider application is the blink reflex. The blink reflex indices are used to differentiate the treatment for pain syndromes related to the oral cavity. Blink reflex, through the stimulation of *n. alveolaris inferior,* has a predictive importance for various sensory disorders of the jaw region or for sensory disturbances related to the orthodontic treatment [10].

The R1 component of blink reflex is achieved through the $A_ß$ fibers that activate low threshold mecanoreceptive (LTM) neurons, probably located in the main trigeminal sensory nucleus. The R2 component appears to stimulate both $A_ß$ fibers and A_δ fibers with the input being in the wide-dynamic range (WDR) neurons, located in the spinal trigeminal nucleus. Interneurons of the R1 wave are located in the trigeminal sensory nucleus and the interneurons for R2 wave in the spinal trigeminal nucleus [11]. Nociceptive stimulation activates A_δ fibers and/or C fibers, then excites *subnucleus reticularis dorsalis* (SRD) neurons with the occurrence of the R3 component. This mechanism is partially involved the R2 component generation. The R3 component has been less studied, its generating mechanisms being still unclear. Unlike R3, the R2 component of the blink-reflex has been quite well researched, currently the neural networks involved in its generation are known; it can be reproduced and can be generated by different stimuli (electrical, thermal, etc.). The R2 component is being used widely in various experimental and clinical studies. It is important that the R1 and R2 indices make it possible to distinguish the non-nociceptive components from the nociceptive ones in the trigeminal system. Facilitation of the R2 component can be observed in migraine attacks, pain related to damage of the trigeminal system, orthodontic pain. Promising results were obtained by applying the blink reflex to differentiate atypical odontalgia.

Temporomandibular joint dysfunction in association with painful syndrome manifests itself by a decrease of the latencies for the R1 component ($p < 0.05$) and for the ipsilateral and contralateral R2 component ($p < 0.0001$) [6,7]. The Wallenberg syndrome changes the R2 wave in 90% of the cases, while wave R1 remains unmodified.

The trigeminal system and the trigeminal reflexes are involved in the pathogenesis of many orofacial pain syndromes. The pain syndrome from the occlusal and temporomandibular disorders, leads to more significant changes in the brainstem area, in comparison with the somatosensory and motor cortical areas [4].

The study of the trigeminal system and features of the trigeminal reflexes will make the development of new diagnostic and treatment technologies possible for patients with orthodontic disorders, that will include both the influence on peripheral components (peripheral electrical stimulation, etc.) and also direct stimulation of brain structures involved in processing the trigeminal reflexes (magnetic or electrical transcranial stimulation, etc.) The current issue is being important for children especially during the process of development and consolidation of various intra- and extra-stomatognathic systems, regarding the possible impact of the orthodontic pathologies.

Material and methods

In this study, there were included 58 children, aged from 9-12 years, who were divided into 2 groups, statistically equivalent by age, gender, facial development degree, presence of a balanced psycho-emotional state. Patients in both groups were examined using traditional clinical exams and complementary exams were completed through neuro-physiological examination of the blink reflex. Clinical exams were performed at the Department of Pediatric Oromaxillofacial Surgery, Pedodontics and Orthodontics at the "Emilian Coțaga" Clinic and at the dental clinic "Orto-Dental" SRL. Electroneurophysiological investigations were executed at the university clinic Neuronova, under the supervision of university professor, academician V. Lacusta. Modern specialized software was applied [20] in conjunction with the neurophysiological equipment – Neuro-MVP (*Neurosoft*).

The neuro-physiological examination methodology for the blink reflex

Blink reflex is a defense reflex that may be caused by applying various stimuli (mechanical, chemical, photostimulation etc.). To obtain this reflex and to conduct the electrophysiological analysis, the supraorbital region is stimulated, at the points of emergence of the first trigeminal nerve branch (supraorbital foramen). The stimulation parameters were: pulse duration of 0.1-1ms, current intensity of 5-15mA, frequency of 0.1 to 0.4 Hz. The reflex was recorded by placing electrodes in the region of the eye muscles. Blink reflex includes the afferent fibers of the trigeminal nerve (the first branch), the efferent fibers of the facial nerve, the nuclei of these nerves, the neurons from the reticular formation of the brainstem [7].

The reflective response contains three components (fig. 1): R1 - oligosynaptic ipsilateral response with a latency of 10-14ms (mainly generated in the pons); R2 - polysynaptic bilateral response with a latency of 25-40ms (*tractus spinalis n. trigeminii*, reticulate formation in the lower brainstem areas); R3 - polysynaptic bilateral response with a 70-100ms latency (intercalary neurons of the brainstem, the neural structures involved in nociceptive control of the gray matter in the area of the midbrain and of the raphe nuclei 5] (fig . 1).

In our studies, we performed a correlative analysis between the R3 indices (presence/absence), the degree of dental anxiety, assessed on the Dental Anxiety Scale according to N. Corah [4] and pain self-assessment indices based on the Visual Analogue Scale (VAS).

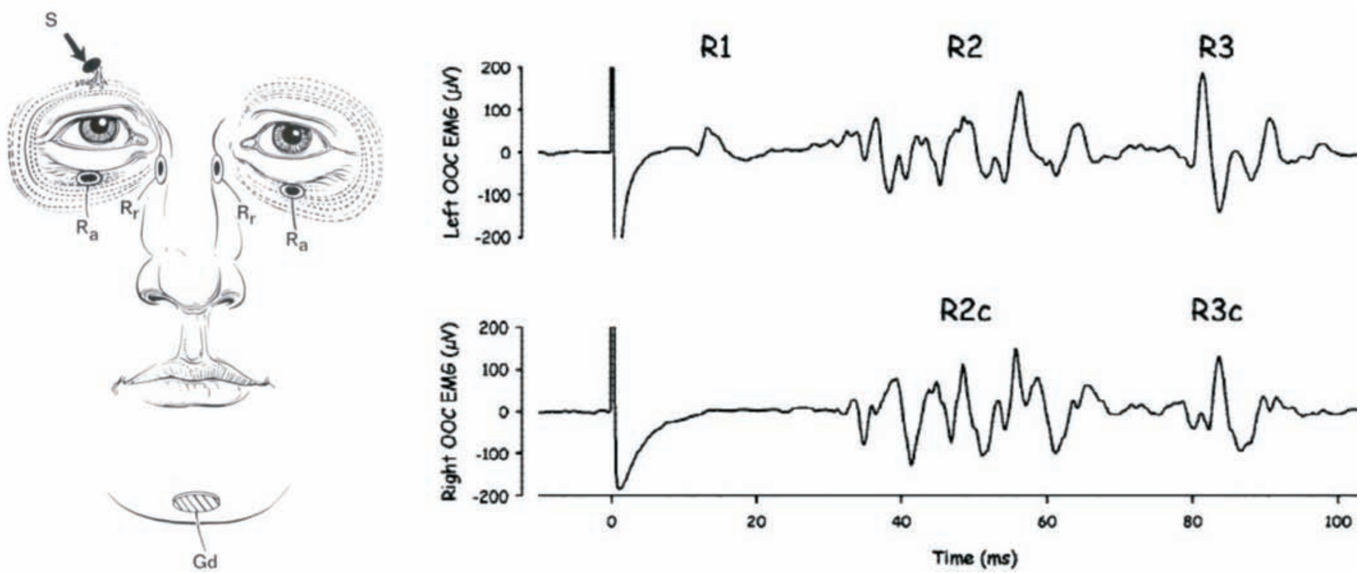

Fig. 1. The R1, R2 and R3 waves of the blink reflex.

Results and discussion

For the analysis of the blink reflex, we have distinguished the R2 component depending on the latency and duration, with a general assessment of the excitability of the involved cerebral structures (tab. 1).

Processing of the blink reflex indices was achieved by assessing the velocity of the nerve impulse conduction in the trigemeno-facial system, the analysis of the segmental brainstem apparatus functional status and by revealing the regulatory influences from the suprasegmental brain structures. Latent wave periods are considered pathological when they are higher than 10.82 ± 1.2 ms for R1, 35.25 ± 3.7 ms for ipsilateral R2, 35.36 ± 3.27 ms for contralateral R2 [1].

Different combinations of the blink reflex indices give the possibility of highlighting the affected brain areas [1,6]: superolateral portion of the pons with the impaired sensory fibers of the trigeminal nerve; anterolateral region of the pons with the impaired facial nerve nucleus and its fibers; the dorsolateral/mediolateral/paramedian/medial regions of medulla oblongata, with the affected region located in the trigeminal nerve fibers at the level of pons (*nucleus sensorius principalis*); location in neurons that connect the ipsilateral and contralateral structures.

These dysfunction variants may be revealed in the process of neurological diagnosis, but their activity is closely associated with the stomatognathic system and nowadays new technologies have been developed that make it possible to use the functional diagnosis for neuro-stomatological pathologies.

The analysis of the blink reflex indices (R1 and R2 waves) has shown that in 34 children with Angle Class III malocclusion (tab. 2), there were significant deviations in comparison with healthy children, which constitutes 58.6% of all investigated patients and that in the post-treatment period, pathological variants of these reflexes were found in 20.7% of cases (12 children).

The diagnostic value of pathological changes of the blink reflex in children with Angle class III malocclusion is not high (specificity 58.3%, sensitivity 49.2%), thus as a single diagnostic method (mono-test), it cannot be used for the studied pathology.

The decrease of the latent period in the R1 wave in children with Angle Class III malocclusion may be explained by the functional disorders at the level of the main trigeminal sensory nucleus and in the neurons of pons. On the other hand, the reduction of the latency of R1 and R2, both ipsilateral and contralateral, may be explained by a more pronounced dysfunction of the trigeminal system, which is present in children with Angle class III malocclusion. This dysfunction according to the literature leads to pronounced changes in the brainstem (trigeminal structures, reticulate formation) the disorders being more severe in comparison with those at the level of cortical somatosensory areas [9,19].

Of all investigated children with Angle class III malocclusion, in 31% of cases (18 patients) the R3 wave was present before treatment, while at three years post-treatment, the R3 wave was found only in 3 children (5.2%). This data reflects the neurophysiological nociceptive/antinociceptive mechanisms at the level of the brainstem and of other suprasegmental structures that had notably improved. The latent period of R3 was 84.61 ± 1.67 ms. It needs to be considered that in the literature

Table 1

General assessment of the excitability

Index	Normoexcitability	Hipoexcitability	Hiperexcitability
Latency, ms	36,9 ± 0,6	39,7 ± 0,5	31,4 ± 0,7
Duration, ms	35,1 ± 0,5	31,2 ± 0,4	49,9 ± 0,8

Table 2

Dynamics of electrophysiological indices of the blink reflex in children with Angle class III malocclusion under the influence of treatment

Parameters/Stimulation/ Values in healthy children (n = 18)	Children with Angle Class III malocclusion (n = 58)	
	Investigation period	Latent period, ms
R1 sinistra stimulation 12,13 ± 0,31	Before treatment	9,49 ± 0,23***
	3 years after-treatment	10,8 ± 0,21**xxx
R2, ipsilateral sinistra stimulation 36,85 ± 0,93	Before treatment	32,53 ± 0,84**
	3 years after-treatment	34,60 ± 1,05
R2, contralateral sinistra stimulation 37,21 ± 1,44	Before treatment	33,94 ± 1,52
	3 years after-treatment	38,88 ± 1,46x
R1 dextra stimulation 12,48 ± 0,29	Before treatment	9,58 ± 0,24***
	3 years after-treatment	11,10 ± 0,80x
R2, ipsilateral dextra stimulation 36,72 ± 0,61	Before treatment	33,08 ± 0,82*
	3 years after-treatment	37,55 ± 0,81xxx
R2, contralateral dextra stimulation 37,43 ± 0,71	Before treatment	33,85 ± 1,07
	3 years after-treatment	38,24 ± 0,78xxx

Note: conclusive statistical differences: for patients with Angle Class III malocclusion vs. healthy children: * - p <0.05; ** - P <0.01; *** - P <0.001; before vs. after the treatment: x - p <0.05; xxx - p <0.001.

there is evidence of the link between the intensity of the pain syndrome and the presence of the R3 wave – disappearance of pain is associated with the disappearance of the R3 wave.

The analysis of the blink reflex waves has been conducted based on the patient's age – with an increase in age, an inhibition deficit appears in the brainstem structures, as well as an insufficient activity of the antinociceptive systems, that leads to the reduction or disappearance of the R3 component. The results of the comparative analysis show a higher frequency of the masseter reflex inhibitor (MIR) disorders in comparison with blink reflex disorders. Nevertheless, this argument is not the main one, as each of these reflexes has specific neural mechanisms and they possess diagnostic value in the context of the applied diagnosis or treatment.

From the literature it is known that patients with occlusal disorders are experiencing increased emotionality during the orthodontic treatment (61.6% of cases), due to the lowering of the pain threshold in the oral mucosa region (71.4%).

In our investigations, for children with the R3 wave of the blink reflex (31% of cases) we analyzed self-assessment of anticipated pain (from a few days before the visit at the doctor until the visit for adjusting orthodontic devices) in comparison with actual pain during the visit and pain experienced in the past (during the last visit at the doctor). The level of anticipated pain (Visual Analogue Scale - VAS) was elevated, which demonstrates a stressful state of anticipation of future visits at the doctor, a fear of possible pain (tab. 3). Some children have rather large pain self-assessment values reaching as high as 7-9 points on the VAS scale. In comparison with the anticipated pain, the real pain showed a statistically significant lower level ($p < 0.05$). The self-assessment of previously experienced pain had lower average values than the self-assessment of anticipated pain ($p < 0.05$).

We performed a comparative analysis of the dental anxiety level, assessed with the aid of Corah Dental Anxiety Scale. In children with R3 wave, the anxiety level has constituted 3.31 ± 0.19 points, and in children without the R3 wave, anxiety had values of 2.37 ± 0.23 – the difference is statistically significant ($p < 0.01$) with greater expression of dental anxiety in the first group. These results demonstrate a connection between the psycho-emotional mechanisms with the processes of R3 wave generation and modulation. In this aspect, of great importance

Table 3

Pain self-assessment by Visual Analogue Scale (VAS) in children with Angle class III malocclusion depending on the presence/absence of the R3 wave of the blink reflex

Patients with Angle Class III malocclusion	Pain self-assessment (VAS)		
	Pain experienced before	Anticipated pain	Real pain
Blink reflex with R3 wave (n = 18)	4,12 ± 0,75+	6,82 ± 1,10*	3,52 ± 1,20+
Blink reflex without R3 wave (n = 40)	4,13 ± 1,96	3,42 ± 0,98+x	3,48 ± 1,81

Note: Statistically significant differences compared to the real pain: * - p <0.05; difference in the group with presence of R3 vs. group without R3 wave: x - p <0.05; difference compared to anticipated pain: + - p <0.05.

is the correlation analysis between the blink reflex waves and the dental anxiety level (tab. 4).

Table 4

Correlation analysis between the blink reflex waves and the dental anxiety level

Rxy: dental anxiety-blink reflex	Rxy	p
R1	0,34	>0,05
R2	0,48	<0,05
R3	0,69	<0,01

The strongest correlations ($p < 0.01$) were found between wave 3 and the level of dental anxiety determined according to Corah Dental Anxiety Scale (fear and feelings of uneasiness, anxiety during the waiting period for the visit at the doctor – for a few days, a few hours, minutes before, anticipation of orthodontic maneuvers while in the dental chair).

As a result of our investigations, it can be concluded that in children with Angle Class III malocclusion, a disorder occurs in the balance of nociceptive/antinociceptive systems with an impact on psycho-emotional processes and on the values of pain self-assessment. According to the literature, the R3 wave is associated with attention focus - if during the investigation of the blink reflex, the patient is prior informed about the stimuli that will be applied, and then the R3 wave is vastly diminishing or even disappears [16]. Williams et al. [21] have shown that for people who have viewed pleasant images (positive emotions) the blink reflex was inhibited and under the influence of unpleasant images (negative emotions); the reflex was facilitated/enhanced. The authors concluded that emotional expression control could influence the blink reflex expression by the intensifying (positive emotions) or diminishing (negative emotions) of the supraspinal inhibition. Sergl et al. [18] observed that orthodontic pain was minimal in people who had self-control of the psycho-emotional state. It has been shown that regarding the experience related to pain, the psychic cerebral matrix is stronger than the pain matrix. Preparing the children with Angle Class III malocclusion before the treatment requires explaining the safeness of the procedures and of the devices to be applied, cultivating a positive emotional attitude and motivation such as to ensure an appropriate patient-physician collaboration. It was shown that such pain-preventing instructions considerably influence the pain intensity.

Our results and literature data make it possible to conclude that in children with Angle class III malocclusion, the fact of identifying the R3 wave in the blink reflex complex will require a special attention concerning assessment of the psycho-emotional state in order to ensure an adequate psychological preparation.

In conclusion, it appears that in the composition of the blink reflex in children with Angle Class III malocclusion, the R3 wave is present in 31% of cases, being associated with psycho-emotional mechanisms of pain inhibition/activation.

Another trigeminal reflex, investigated by us, in children with Angle class III malocclusion was the trigemino-cervical reflex (TCR). In recent years, particular attention is drawn upon the interaction between the stomatognathic systems with other systems (stomatognathic-extra-stomatognathic interaction). A special role in this aspect has the interaction of the stomatognathic system with the cervical muscles, because the pathologic trigemino-cervical reflexes are present in various neurological and neuro-stomatological disorders. Analyzing the recent literature, we found that the current investigations regarding the trigemino-cervical reflex (TCR) under physiological conditions are performed mainly experimentally on animals without any clinical data. There is a necessity of investigations of this reflex, in particular for children with Angle Class III malocclusion, because in this pathology, various polymorphic disorders occur in the stomatognathic system, as well as in the cervical region (trigemino-vascular disorders, etc.). It is known that disorders of trigemino-cervical system, along with the trigemino-vascular system are one of the main causes for various headaches.

Disorders of the trigemino-cervical neuronal system lead to headaches and migraines [1]. Accordingly revealing the multidirectional pathogenic pathways between the trigeminal structures and the cervical region is a current problem, the solution to which will contribute significantly to optimization of the differential diagnosis and will ensure an adequate treatment, not only of malocclusions, but also for associated pain syndromes. It was established that not only the pathogenic influence from the stomatognathic system is important, but also vice versa – disorders of the cervical region give rise to pain in the jaws and jaw muscles. Some of latency periods of the trigemino-cervical reflex resemble the ones from the masseter inhibitory and blink reflex. This aspect of the problem is being studied experimentally, due to the fact that when there are essential differences between latency periods of the TCR and that of the R1 blink reflex wave, more severe disorders are occurring [12]. Based on experimental studies, trigemino-cervical reflex is considered a sensitive test for neuromuscular, trigemino-cervical disorders. Moreover, using TCR can reveal pathologies that are not diagnosed on EMG.

Conclusions

1. The manifestation frequency of pathological trigeminal reflexes in children with Angle class III malocclusion increases in this order: trigemino-cervical reflex (41.4%) → blink reflex (58.6%) → masseter inhibitory reflex (93.1%); masseter inhibitory reflex has the diagnostic value for children with Angle class III malocclusion of 85.5% (specificity) and 81.2% (sensitivity).

2. Under the influence of the treatment, in children with Angle class III malocclusion, the frequency of manifestation for pathological trigeminal reflexes decreased by 46.7% for the masseter inhibitory reflex, 37.9% for the blink reflex and 8.6% for reflex- trigemino-cervical reflex.

3. In children with Angle class III malocclusion, in the blink reflex complex, in 31% of cases the R3 wave is present, which is associated with psycho-emotional mechanisms of inhibition/activation for anticipated pain.

4. Perspective future research in children with Angle class III malocclusion needs to be focused on uncovering the correlation between the expression degrees of trigeminal

reflexes with the functional disorders in the stomatognathic and extra-stomatognathic systems (vestibular functions, pain syndromes, etc.)

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