

The role of the red nucleus in the switching of the descending supraspinal influences

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To advance the present-day understanding of descending command signals for posture and movement, there is need for more thorough knowledge of the anatomy and physiology of neurons whose axons descend from the brainstem into the spinal cord. Regulation of motor activity is to a greater extent determined by the interaction of various descending motor systems. On the basis of clinical results pyramidal (corticospinal) and extrapyramidal systems were distinguished. Among various components of the latter a special place belongs to the rubrospinal tract [11,36]. This is conditioned by a greater similarities in the structural and functional organizations of corticospinal and rubrospinal tracts [9,17], being components of lateral system of descending spinal pathways [28]. The functional properties of these two motor systems revealed similarities in regulation in such parameters as velocity [9,17,18], time of involvement, direction [10,17] and force [10,15,17] of movements. It has been shown that the terminals of corticospinal and rubrospinal pathways may overlap in the same spinal layers and may synapse on the same neurons [6,20,22]. Physiologically, the same effects are also described as originating from the two tracts [52].

It is supposed that both the descending systems are in hierarchy as the sensorimotor cortex projects to spinal cord directly and indirectly through the red nucleus (cortico-rubrospinal pathway). The pyramidal tract, passing through the brainstem gives a significant number of collaterals to the brainstem structures [39,43,46]. The pyramidal tract proper or corticospinal tract represents the part of pyramidal tract, which leaves the brainstem [42]. The extending collaterals are the potential pathways of the "extrapyramidal type" and provide the brainstem structures copy of cortical motor output. Impulses, generated by neurons of corticospinal tract may be fed into number of structures of brainstem having extrapyramidal origin including that giving rise to the descending pathways and therefore a clear distinction between py-

ramidal and extrapyramidal systems loses its functional significance [41].

According to another assumption, it is not excluded that corticospinal and rubrospinal tracts constitute parallel systems, acting relatively independent on spinal neurons. Such parallel systems can function to control the various aspects of motion. The prevailing participation of corticospinal system during the training of animals of new motor tasks [40] and activation of cortico-rubrospinal system during an already learnt automatized movements was demonstrated [37]. Both the proposals can be accepted in relation to the working hypothesis.

Red nucleus is a key structure in the premotor system of regulation of the motor activity in the vertebrata. The comparative morphological analyses have shown that the red nucleus and rubrospinal tract arise in vertebrata with appearance of limbs or limb-like structures, and that a number of neurons in the red nucleus increase with the development of tetrapod locomotion [47]. There is a parallelism in the development of the descending pathways and motility of animals. The use of all limbs coincides just with the period when rubrospinal tract reaches spinal cord. While improving skilled movements, to observe increasing of lateral cerebellum, its connections with the cerebral cortex and the prevalence of the parvocellular part of the red nucleus over its magnocellular part are observed. The increase in the repertoire of movements is accompanied by the involvement of higher level of integration, represented by projection of hypothalamic, pretectal, subthalamic, geniculate and other structures to the red nucleus [24,35]. These projection systems phylogenetically precede the origin of the motor cortex and pyramidal tract. The appearance of the latter is a sign of an absolutely new stage of regulation of the large motor descending system of the red nucleus, serving as the basis for co-ordinations of cerebellar and cortical sending in the control of movements. The findings of experiments on the role of the red

nucleus in the interaction of corticospinal and corticorubrospinal systems are considered below.

The results of the mechanism of switching the descending corticospinal and corticorubrospinal influences on the motor activity are shown. The experiments were performed on 2-3 months old albino rats, weighing 210-250g, which had been trained for the instrumental reflexes for balance ability. The experiment was performed on three groups of animals.

The dorsolateral funiculus, through which the rubrospinal tract passes, was transected in the rats of the first group after training for stable instrumental reflexes on the 2-4th days (mean 2.5 ± 0.5 ; $n=67$) (first series). The transection was performed in the region of the cervical segments of spinal cord (C3), which resulted in the paresis of homolateral fore- and hindlimb within five to seven days. On days 5-7 the conditioning for instrumental reflexes resumed and became stable on the 4-13th days (mean 8.3 ± 3.9 ; $n=27$). In the rats of the second series with stable instrumental reflexes the unilateral RN was lesioned electrolytically. It resulted in the disturbance of motor activity of the fore- and hindlimb contralateral to the lesioned side. On the 5-10th days postoperatively, after compensation of the motor deficit (the intensity of the motor deficit depended on the degree of red nucleus destruction), the training for instrumental reflexes was resumed and the stable reflexes were revealed on the 17-22d experimental days (18.3 ± 3.2 ; $n=6$). In the third series of the experiments, in the rats of the first group on the 16-17th days after unilateral transection of the rubrospinal tract, the contralateral red nucleus was lesioned electrolytically. It resulted in motor disorders, which were observed after isolated destruction of the red nucleus. The training for instrumental reflexes was resumed on the 7-10th days after the operation. The reflexes became stable on the 12-16th days (mean 14.2 ± 0.5 ; $n=6$) [13]. During these experiments electrolytic lesion of RN resulted not only in a damage of the red nucleus neural elements, but also in interruption of the cerebellothalamic fibers passing through the red nucleus to the ventrolateral thalamic nucleus and giving collaterals to rubral neurons. In this connection the experiments were performed (the fourth series), which consisted of chemical lesioning of RN by injection of quinolinic acid (Sigma) into it, which destroyed the soma of red nucleus neurons, whereas cerebellothalamic fibers were preserved. These experiments showed that after a chemical lesion of red nucleus the motor disorders were compensated, and the stable instrumental reflexes were recovered on the 18-27th days (mean 22.2 ± 3.4 ; $n=4$). At the same time during the experiments that involved the preliminary transection of the rubrospinal tract and the subsequent chemical lesion of red nucleus, the stable instrumental reflexes were recovered on the 6-10th experimental days (mean 8.25 ± 1.6 ; $n=4$). The application of the method of labeled horserad-

ish peroxidase (Type, Sigma) at the end of the experiments showed the destruction of the somata of rubral neurons and preservation of cerebellothalamic fibers passing through the red nucleus.

The experiments showed the facilitating influence of preliminary transection of the rubrospinal tract on the recovery of motor activity and of instrumental reflexes after lesion of the red nucleus [26,27]. The facilitation time was revealed as the difference between the times of recovery of instrumental reflexes after red nucleus lesion alone and after lesion of the red nucleus preceded by transection of rubrospinal tract. In case of electrolytic lesion of red nucleus indicated time prolonged to 4.1 (18.3 - 14.2) or 5.8 days (20.0 - 14.2), under the chemical lesion - 14.0 days (22.2 - 8.25) ($p < 0.005$). Consequently facilitating influence of the preliminary transection of rubrospinal tract during chemical lesion of RN was more pronounced than during its electrolytic lesion, which should be explained by preservation of cerebellothalamic fibers to ventrolateral thalamic nucleus [14].

On this basis, a faster recovery of rubral lesion after preliminary transection of rubrospinal tract, in comparison with isolated lesion of RN is considered to be the result of the activation of the rubro-olivary projections, leading to the switching of motor activity under the control of the corticospinal tract. This reorganization is accomplished by involvement of the cerebellum and the ventrolateral thalamic nucleus, transferring information to the cerebral cortex. A lesion of the red nucleus without preliminary transection of rubrospinal tract completes with greater disorders, because such interference leads to the simultaneous dysfunctioning of the rubro-olivary and rubrospinal tracts, and therefore there is no switching to the corticospinal tract.

In another series of experiments (the fifth) in the rats that had been trained for stable reflexes the ventrolateral thalamic nucleus was lesioned electrolytically, since the ventrolateral thalamic nucleus is one of the key structures in switching of descending influences. In operantly conditioned animals the motor disorders of the contralateral half of the body weakened on the 5-10th days after operation and stable instrumental reflexes were revealed on the 17-21st days (mean 19.8 ± 2.1 ; $n=7$). In the sixth series of experiments in the rats a preliminary transection of the rubrospinal tract was performed and on the 15-23d days the ventrolateral thalamic nucleus had been lesioned electrolytically. Instrumental reflexes became stable on the 5-13th days (mean 9.1 ± 3.1 ; $n=6$). Thus, in these experiments the facilitating influence of preliminary transection of the rubrospinal tract on the recovery of instrumental reflexes and compensatory processes were revealed after lesion of ventrolateral thalamic nucleus. In the seventh series of experiments in 11 rats the ventrolateral thalamic nucleus was lesioned before training for instrumental reflexes. In the future in these animals transection of the

rubrospinal tract and red nucleus lesion were performed consequently. Following for dynamic behavior showed, that in the rats with the lesion at ventrolateral of corticospinal tract is very hampered. The lesion of the ventrolateral thalamic nucleus essentially weakened instrumental reflexes, which became unstable after transection of the rubrospinal tract and the reflexes were not revealed after the lesion of red nucleus in some animals. Preliminary lesion of ventrolateral thalamic nucleus practically deprives the cerebral cortex of ascending, signaling the defects of cerebellar influence on corticospinal system, without which the controlling and the correcting functions in descending influence on motor apparatus are hampered.

In the second group of experiments the possibility of switching of activation of rubro-olivary projections with corticospinal systems (in case of its lesion) onto corticospinal systems was observed. For this purpose a model of experiments was elaborated for observing the influence of preliminary unilateral transversal transection of bulbar pyramid (pyramidotomy) on the behavior and compensatory-recovery processes in the rats after ablation of the sensorimotor cortex on the same side. The experiment of the first series showed, that in the rats with stable instrumental reflexes the pyramidotomy leads to its disorders during 3-7 days (mean 3.9 ± 1.3 ; $n=7$). Subsequent unilateral ablation of the sensorimotor cortex resulted in a deeper disturbance of motility of the animals with severe paresis of contralateral limbs. Instrumental reflexes became stable on the 7-11th days after operation (mean 9.2 ± 1.8 ; $n=7$). In the second series of experiment in the rats, which had been trained for stable reflexes, isolated unilateral ablation of sensorimotor cortex was performed. After this operation the reflexes became stable on the 14-26th days (mean 19.0 ± 5.9 ; $n=5$). Consequently, preliminary pyramidotomy showed exact facilitatory influence on the recovery of motor activity and on the instrumental reflexes after ablation of sensorimotor cortex (compare 19.0 and 9.2 days).

In the third group of the animals the effects of pyramidotomy onto the instrumental reflexes in rats, depending on the time of its realization was observed. Preliminary pyramidotomy had been performed in the animals and after recovery of neurological status, the training for instrumental reflexes started. The stable reflexes were trained on the 14-24th days (mean 16.5 ± 3.16 ; $n=8$). The comparison of the results of the second and the third groups of rats showed a great difference in the time of stabilization of instrumental reflexes (compare 3.9 and 16.5 days) (statistically significant at $p < 0.005$). The time of pyramidotomy was the determining factor. The difference in these two groups was revealed even after the subsequent ablation of sensorimotor region of cerebral cortex. In the rats of the second group, as it was mentioned, instrumental reflexes became stable after cortical ablation on average on the 9.2th days, whereas in the rats of the

third group they became stable only on the 11-29th days (mean 21.4 ± 6.3 ; $n=5$). Consequently, the phenomenon of enhanced corticofugal plasticity, exactly being revealed as the result of pyramidotomy in the adult rats disappears totally after preliminary transection of corticospinal tract.

The most probable system involved in the liquidation of the pyramidal deficit, during the compensation of motor and behavioral disturbances after pyramidotomy is the cortico-rubrospinal system, which is determined by great similarities in the structural and functional peculiarities of these both descending systems. The deficit, produced in one of these two systems is transitory and the functional recovery is realized as the result of capability of the non-damaged system to take control of the movement. The leading factor in the described phenomenon is the interaction of corticospinal and cortico-rubrospinal systems, their properties of inter-substitution being unique among all the descending motor systems. It should be noted that the switching activity of rubro-olivary projections can be carried out in both direction, and in case of damaging of general property mentioned above is that a preliminary lesion of a peripheral part of a system, represented by a descending spinal projection (corticospinal and rubrospinal), facilitates the compensation of the central part during its subsequent distraction.

Corticospinal and rubrospinal tracts are in "concurrent" and simultaneous in "duplication" relationships. The cerebellar messages can control their activity through the cerebral cortex and the red nucleus. The cerebellar outputs reach various cortical zones mainly through the ventrolateral and the ventroanterior thalamic nuclei (motor thalamus) [13]. The cerebellum can influence the rubrospinal and rubro-olivary tracts through its direct projections onto the red nucleus [36]. At the same time the red nucleus receives massive projection from the ipsilateral sensorimotor and parietal cortex [12, 21]. Therefore, the red nucleus possesses the descending pathway totally for impulse, arising from cerebellum and motor cortex. Cerebellar and cortical inputs are topographically organized overlap widely. As a result motor outputs can be modulated by informational convergence from both the sources [1,16,22]. In this case the rubrospinal tract appears as the general pathway for cortical and cerebellar messages. The cerebellar and cortical inputs of the red nucleus and its spinal and all olivary projections are ordered somatotopically. The neuronal responses of the motor thalamus and the red nucleus are strictly correlated with motion and as a rule, start before the movement [2,3,33, 51]. Thus, both the rubrospinal and corticospinal tracts are largely under the control of the cerebellum [23,38]. Both tracts can interact via numerous loops at the cortical, the brainstem and the spinal levels. Both tracts send projections to various levels to spinal cord [36].

Rubrospinal neurons are distributed along the whole rostrocaudal extent of the red nucleus of the rats [26,45].

Moreover, all types of neurons of the red nucleus project onto the inferior olive [26]. In the rats the rubro-olivary projection is the collateral of the rubrospinal tract [25]. However, in future evolutionary there is a demarcation between rubrospinal and rubro-olivary projections. For example, in primate red nucleus there is progressive expansion of the phylogenetically newer rubro-olivary projection at the expense of its rubrospinal counterpart. The rubro-olivary subpopulation displaces almost completely the rubrospinal subpopulation in apes and in humans.

As it has been mentioned, the prevailing participation

of corticospinal systems during the training for new motor tasks was shown [41]. As the movements are learned, their execution become automated under the control of rubrospinal tract [37] as a result of the switching activity of rubro-olivary projection. The experiments of damaging of corticospinal and rubrospinal tracts show, that there is a considerable duplication between them. The deficit produced in one of them is just transitory [31] and the functional recovery occurs as a result of the capability of the nondamaged system to take control of the motion [8,30,32-34]. In case of damage to both the tracts a severe

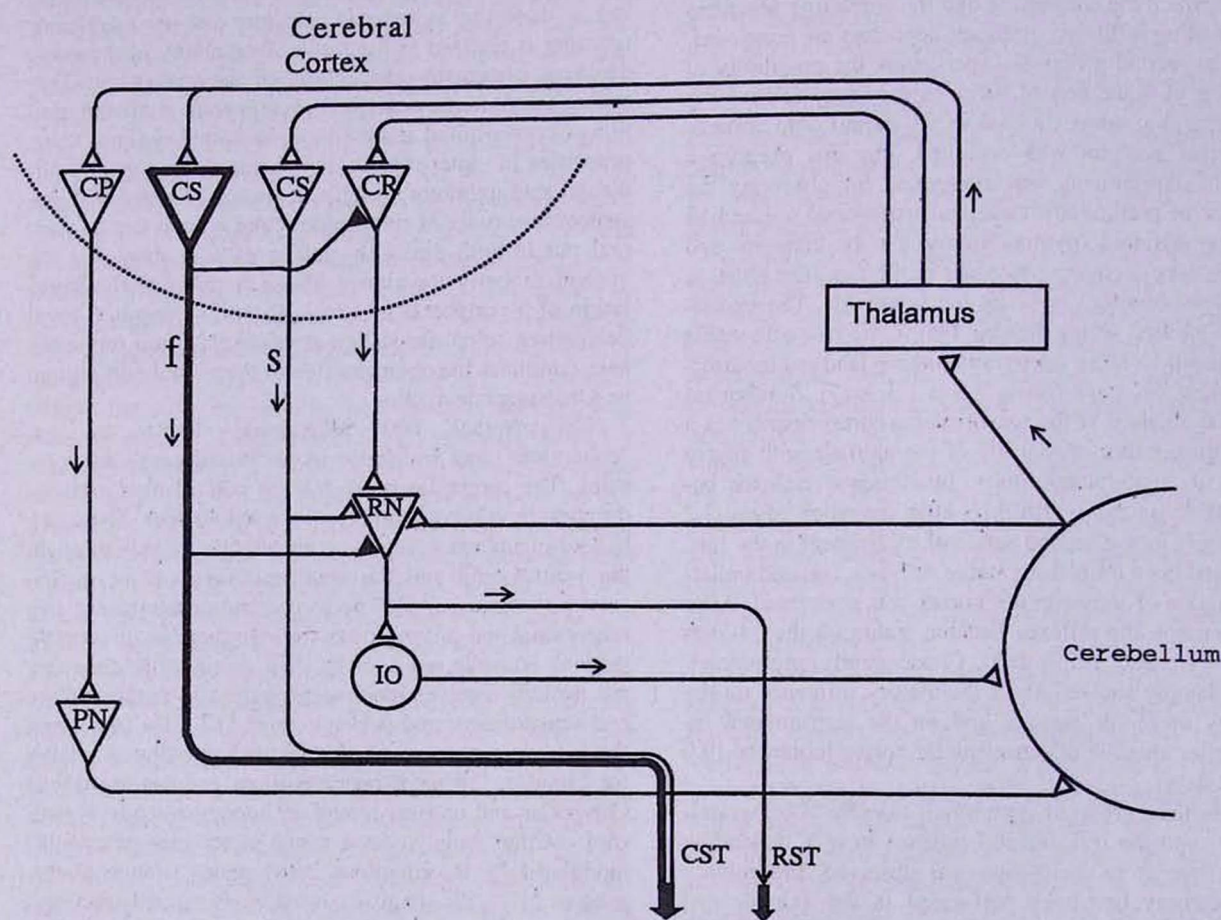


Figure. Basic circuit diagram for the interrelation and substitution of corticospinal and cortico-rubrospinal systems. Corticospinal (CST) projections arise from fast-conducting (CSf) and slow-conducting (CSs) pyramidal tract cells. Corticorubral projections arise from corticorubral (CR) cells within the cortex. CSs and CR are connected monosynaptically with rubrospinal tract (RST) cells of the red nucleus (RN). Neurons of RN receive cerebellar input via the deep cerebellar nuclei, which are dichotomized axons projecting to the cerebral cortex through the thalamus. Rubro-olivary projections are terminated on the inferior olive (IO), which send olivocerebellar fibres to the cerebellar cortex and cerebellar nuclei. CSf exert inhibitory influences on CR and RST cells. Corticopontine projection neurons (CP) to the pontine nuclei (PN) provide polysynaptic connections from the cerebral cortex to the cerebellum. CSf are indicated by thick line. Excitatory and inhibitory projections are shown as open and filled knobs. Arrows show the direction of ongoing information.

and persisting deficit is produced [11], which can be not even compensated [29]. The corticospinal tract receives cerebellar sendings through the cerebello-thalamo-cortical relay. The cerebellar influences cover a wider region in the cerebral cortex than the area from which the corticospinal projections take the origin. In parallel, the cerebellum receives the mossy fiber inputs from all the cerebral cortex. It is obvious, that the cerebrocerebellar communication loop not only assists the corticospinal tract, but also serves a wide variety of cerebral cortical functions [19].

The general property of models mentioned above is that a preliminary lesion of a peripheral part of a system, represented by a descending spinal projection (corticospinal and rubrospinal), facilitates the compensation of the central part during its subsequent distraction. The switching mechanism of both observed descending projection pathways schematically are shown in the Figure. The corticospinal tract (CST) takes the origin from the fast (CSf) – and slow-conducting (CSs) corticospinal (pyramidal) tract cell. The cortico-rubral projection takes the origin from the cortico-rubral cell (CR) of cerebral cortex, which are monosynaptically connected with the neurons of rubrospinal tract (RST) of the red nucleus (RN). The latter also receive monosynaptical excitatory influences from CSs, cerebellar deep nuclei (interpositus and lateralis). The polysynaptical excitatory influence of cerebral cortex on the red nucleus can be provided by cortico-ponto-interposito-rubral pathway (CP,PN). It should be noted that cortico-ponto-cerebellar loop is one of the more pronounced pathways in the mammalian central nervous system. Evolutionary its formation went parallel with the development of the cerebral cortex hemispheres and cerebellum and was accompanied by improvement of motor skills [44]. In human being the number of cortico-pontocerebellar fibers is total 40 millions [48]. The slow-conducting pyramidal tract fibers and cortico-rubral fibers ending in the periphery dendritic of the red nucleus neurons induce slow monosynaptic dendritic EPSPs [50]. The fast-conducting pyramidal tract neurons via axon collaterals produce inhibition (IPSPs) in the red nucleus neurons with disynaptic latencies through inhibitory interneurons within the red nucleus. It is important to note that the fast-conducting pyramidal neurons also have an inhibitory influence on cortico-rubral cerebral neurons (CR) [49]. Therefore, the cortico-rubrospinal pathway can be inhibited at two levels: the cerebral cortex and the red nucleus. Thus, in a normally functioning brain a switching mechanism is proposed according to which the cortico-rubrospinal system is silenced by inhibition at the level of the cerebral cortex and the red nucleus, when the fast-conducting pyramidal tract cells are activated. These in-

hibitory effects are weakened after the completion of training for a new motor activity, which is accompanied by transfer of the latter under the control of the cortico-rubrospinal systems for automatically execution. In case of exclusion of the corticospinal systems as a result of its destruction the cortico-rubral system receives a greater volume of freedom, giving opportunity for compensation of the absent effects of pyramidal tract. The switching mechanism from the corticospinal to the cortico-rubrospinal system, acting under normal conditions during the transfer of a newly conditioned movement into the automatized regime under the control of cortico-rubrospinal systems seems to be one of the key events in the compensation of a deficit, produced by the lesioning of pyramidal tract. The same mechanism also has effect in case of the damaging of rubrospinal tract. The involvement of other mechanisms, such as activation of cortico-cortical and interhemispheric connections and also the involvement of the tracts of the medial descending systems (reticulospinal, vestibulospinal, tectospinal) [31] in compensation of the deficit of the central part, if it is represented by the red nucleus, sensorimotor cortex or ventrolateral nucleus of thalamus is not excluded.

The represented material fully concerns the problem of the center and periphery in the physiology of nervous activities, which origin elaboration was mainly appointed in the first decade of the twentieth century [4,5,7]. The indicated problem is closely connected with the analysis of destroyed function compensation mechanism. The scientists paid special attention to the elucidation of the compound complex of influence from the central nervous system and afferent impulses, taking the origin from executive organs. The mechanisms of reorganization, rebuilding, "retraining" of nervous center were investigated. The peculiarities of periphery and central processes interconnections and the regulating role of constant signaling periphery in the integrative function of the central nervous system was analyzed. The above expounded material makes it possible to elucidate the problem of the center and periphery from the other side; from the standpoint of correlation of the periphery and central parts of efferent systems, when the disturbance of the periphery acquires signal forestalling significance for mobilization of compensatory ability of brain with the purpose of recovery of the deficit of the central link of the system.

Կարմիր կորիզի դերը ողնուղեղային վարընթաց ազդեցությունների փոխանցման գործում

Վ.Բ. Ֆանարջյան

Կարմիր կորիզի ողնուղեղային ուղու մախնական ընդլայնական հատումը հեշտացնում է գործիքային ռեֆլեքսների վերականգնումն ու հարմարողական գործընթացները, որոնք ընթանում են սպիտակ առնետների կարմիր կորիզի կամ փորակողմային կորիզի քայքայումից հետո: Նմանակերպ կոնդեզային բրգի մախնական միակողմանի հատումը արագացնում է գործիքային ռեֆլեքսների վերականգնումն ու հարմարեցումը շարժողական պակասությունը, որը տեղի է ունենում մույնակողմ զգայաշարժ կեղևի հեռացման հետևանքով: Նշված երևույթը կապված է

կարմիր կորիզ-ձիթապտուղ պրոեկցիաների ակտիվացման հետ, որը առաջատար դեր է ստանձնում վերողնուղեղային վարընթաց ազդեցությունների փոխանցման գործում:

Առաջ է քաշվում դրույթ, համաձայն որի ողնուղեղային վարընթաց պրոեկցիաների ծայրամասային բաժնի վնասումը ձեռք է բերում ազդակային մշանակություն ուղեղի փոխհատուցման հարմարեցման հավաքագրման կենտրոնական օղակի պակասության փոխհատուցման մախնակով:

Роль красного ядра в переключении нисходящих супраспинальных влияний

В.В.Фанарджян

Предварительная поперечная перерезка руброспинального тракта облегчает восстановление инструментальных рефлексов и компенсаторные процессы, наступающие после разрушения красного ядра или вентролатерального ядра таламуса у белых крыс. Подобным образом предварительная унилатеральная перерезка бульбарной пирамиды ускоряет восстановление инструментальных рефлексов и компенсацию двигательного дефицита, имеющего место после удаления ипсилатеральной сенсомоторной коры. Отме-

ченный феномен связывается с активацией руброоливарной проекции, играющей ведущую роль в переключении нисходящих супраспинальных влияний.

Выдвигается положение, согласно которому предварительное повреждение периферической части нисходящей спинальной проекции приобретает сигнальное значение для мобилизации компенсаторных способностей мозга с целью компенсации дефицита центрального звена системы.

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