

NEURONAL MECHANISMS OF CORTICO-RUBROSPINAL SYSTEM

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Red nucleus (RN) is an important link in the output of cerebellocortical loop integrating descending signals from those two suprasegmental structures [29,39,44]. Evolutionarily the origin of RN and, especially, its main descending pathway, i. e. rubrospinal tract is connected with the presence of limbs or limb-like structures in animals [6,26,48]. Of great significance for the development of the mentioned structures characteristics is the evolution of cerebellorubral projection and later, in higher mammals, evidently, the powerful development of corticospinal tract and neocerebellum [2,4]. Cerebellar and cortical projections are principal inputs of RN in mammals [9,10]. The RN participation in four coordinating processes reflecting different levels of motor behavior integration will be considered below. These are successive and complementary processes which define certain characteristics of RN neuronal mechanisms activity.

Switching descending corticospinal and rubrospinal influences

Cortico-rubrospinal system is very much like corticospinal one in controlling distal limbs muscles [4,5,25]. Both systems are somatotopically projected towards all brain levels. Both systems have common cortical fields originating from cerebral cortex [15,52]. Cortico-rubrospinal system has motor functions similar to those of corticospinal neurons. Defects caused by the injury of one of the tracts are well compensated by the intact tract, which suggests the presence of a common functional organization in them. Monkeys have been shown to have a tendency to restore a voluntary control over limbs after uni- and bilateral pyramidotomy, which disappeared after the lesion of RN or rubrospinal tract [33]. Rubrally caused movements are similar to those evoked by stimulation of corresponding cortical fields [32]. Spinal terminals of corticospinal and

rubrospinal tract overlap on the laminae V-VII of Rexed. Axons of both tracts end on the one and the same type of segmental interneurons as well as on propriospinal neurons [28]. Both tracts facilitate flexor motoneurons and inhibit extensor motoneurons [23,42]. Under comparative analysis of descending influences great similarity of functional properties in these two motor systems in regulating parameters such as velocity, time of involvement and force of movements has been shown [5,25]. Apart from this predominant participation of corticospinal neurons in animals learning new motor skills and activation of rubrospinal neurons when performing previously learnt automated movements have been noted [35,40]. The idea according to which the switch in activity of these two descending tracts is realized by rubroolivary system [30,31] and cerebellum [27] has been advanced.

In operantly conditioned rats the unilateral transection of rubrospinal tract and further lesion of RN or ventrolateral nucleus of thalamus leads to fewer motor and behavior disturbances than the isolated initial lesion of RN or ventrolateral nucleus of thalamus alone [27,30,31]. Preliminary transection of rubrospinal tract is supposed to serve as a signal for switching motor activity. After lesion of rubrospinal tract, rubroolivary projection gets activated owing to which the switch of motility under the control of corticospinal system takes place, which compensates for the deficit of destruction of RN. This reconstruction is assumed to be realized due to the involvement of rubroolivary projection [31] and cerebello-rubroolivary triangle [27]. Further involvement of corticospinal tract is implemented via activation of ascending loop coming from inferior olive to cerebellum-ventrolateral thalamic nucleus cerebral cortex [17]. One and the same efferent cells of cerebellar nuclei have been shown to be projected into RN and ventrolateral nucleus of thalamus [3,47], which makes it possible to send identical cerebellar signals to corticospinal and rubrospinal neurons. In this scheme ventrolateral thalamic nucleus is a principal transmission link of ascending cerebellar influences on cerebral cortex due to which the latter gets involved into a new context of movements. However, additionally this type of cerebellar ascending influences on cerebral cortex could be realized via other cerebellocortical pathways as well. The latter could involve nucleus ventralis anterior, non-specific nuclei of thalamus and reticular formation of brainstem [9,18,27].

The influence of corticospinal and corticorubral cells on rubrospinal neurons

There is a coordination between corticospinal and cortico-rubrospinal systems. Pyramidal cells have been shown to inhibit (occasionally activate) neighboring corticorubral neurons of sensorimotor cortex through recurrent axon collaterals. The inhibition of corticorubral neurons is expressed in generation of inhibitory postsynaptic potentials (IPSP) and in cessation of their spontaneous discharge. This causes disfacilitation of rubrospinal neurons [50]. Antidromic activation of medullary pyramidal tract evokes excitatory postsynaptic potentials (EPSP) and IPSP in rubrospinal neurons of ipsilateral RN. Large phasic cells of pyramidal tract have been shown to inhibit (via interneurons) and

small tonic cells of the same tract have been shown to excite RN neurons through its axon collaterals in midbrain [50].

The study of interaction between corticospinal and corticorubral systems under their influence on RN has been carried out with the help of analyzing postsynaptic potentials evoked in rubrospinal neurons on stimulation of cerebral cortex. The possibility to evoke complex multicomponent EPSPs on descending cortical signals as opposed to simple monocomponent EPSPs on cerebellar signals has been demonstrated.

Complex corticofugal EPSPs have been recorded in 2/3 of the studied rubrospinal neurons. Components of those EPSPs have been distinguished using cortical stimulation of various intensity and frequency.

The first early component of the EPSP appearing at the lowest threshold was found to have a short and stable latency, stable rising time for depolarization and was able to follow high frequencies of stimulation. The second component was more variable, although in some EPSP it too had a short latency which was stable enough and, like the first component could be classified as monosynaptic. The complex character of the EPSPs recorded persisted after the removal of the cerebral gray matter and was observed when stimulating the white matter so excluding its cortical origin. The first two components of the EPSP were evoked by corticofugal impulsation propagating at average velocity of 18.5 m/s and 7.5 m/s being supposed the result of activation of the slow-conducting pyramidal and corticorubral neurons [11]. By means of selective activation of corticospinal fibers at the level of medullary pyramids and by studying peculiarities of their interaction with the effects of cortical stimulation, participation of corticospinal input in initiating the above-mentioned EPSPs has been determined. Convergence of excitatory influences from sensorimotor cortex and medullary pyramids has been observed in 94.2% of the rubrospinal neurons studied. In some neurons (8.1%) the summation effect of cortical and pyramidal inputs was 100% which suggests that the corticorubral neurons play a predominant role in the genesis of cortical EPSPs. In the majority of cells, the summation of inputs tested was less than 100%, proving that both corticospinal and corticorubral neurons participating in initiating the EPSP were evoked by cortical stimulation. A collision component consisting of the difference between the algebraic and experimental sum of the EPSPs and reflecting that part of the depolarization which "dropped out" of the summed EPSP as a result of impulse collision in pyramidal fibers carrying stimulation effects from both the sensorimotor cortex and the medullary pyramids, was distinguished when studying interactions between the inputs mentioned above. From computer analysis it was possible to assess separately pyramidal and extrapyramidal participation in corticofugal control. Depolarization "dropped out" as a result of collision of impulses in pyramidal fibers making 58.3% for the first and 53.3% for the second component. Thus, it has been established that slow-conducting corticospinal and corticorubral neurons equally participated in initiating the first two components of complex EPSP [12,13].

Cortical and cerebellar control of rubrospinal neurons activity

Principal afferent inputs of RN from sensorimotor cortex and cerebellar nucleus interpositus have different termination on rubrospinal neurons. Morphologically cortical projections end on distal dendrites, whereas cerebellar fibers establish direct contacts with soma and proximal dendrites of rubrospinal neurons [36,37]. This difference is clearly observed in electrophysiological investigation of the mentioned projection effects. Rubrospinal neurons' monosynaptic EPSPs evoked by stimulation of cerebellar nucleus interpositus are characterized by a quick rise time of depolarization and relatively short total duration. On reaching a critical EPSP level, action potentials (AP) are generated in all rubral neurons. The unique feature of the cerebellorubral synapses is the high degree probability of transmission of the excitation expressed in the absence of dropping-out of responses on stimulation of the single fibers of nucleus interpositus as well as in the fact that neither depression nor facilitation are observed in the cerebellorubral transmission on the paired and tetanic stimulation of the nucleus interpositus [49]. However, apart from this, interpositorubral connection has synapses the efficiency of transmission through which changes at sending successive stimuli [20]. On the basis of the study of elementary EPSP of RN neurons it has been shown that transmission efficiency modification in the cerebellorubral pathway is connected with plastic changes in synaptic functioning and does not reflect changes in presynaptic flow of impulses.

Cerebellar nucleus interpositus being the main source of afferents to rubrospinal neurons has been shown to receive a reverse projection from these neurons. Morphologically rubrocerebellar projection is somatotopically organized and ends in central nuclei and cerebellar cortex [7]. It has been established electrophysiologically, that rubrocerebellar projection originates from two RN neuronal populations: the rubrospinal ones, being formed from their axons' collaterals and the independent group of cells which are not rubrospinal and do not have synaptic inputs from cerebellar nucleus interpositus and in the majority of them, from cerebral cortex [21].

A different picture is typical of rubrospinal neurons' corticofugal monosynaptic EPSP. They are characterized by a slow duration. The depolarization reaches maximum in 4-5 times longer period than one necessary for cerebellofugal EPSP [16,51] in one and the same rubrospinal neurons. Slow corticofugal EPSPs are not sensitive towards artificial polarization of neurons. Evidently, non-linear summation of unitary EPSPs takes place in dendrites in which owing to the high input resistance they reach a considerable value. Frequently on reaching a critical depolarization level AP characterized by irregular exposure have been generated in RN neurons [51]. The most probable mechanism of their appearance is an electronic propagation of gradual depolarization from dendrites into the area of initial segment. This should have been facilitated by morphological peculiarities of rubrospinal neurons having a radial disposition of principal dendrites.

Monosynaptic EPSPs in rubrospinal neurons have been also registered on stimulation of parietal association cortex [19,22]. The analysis of summary and elementary EPSPs has shown that according to their time parameters they occupy an intermediate position between those originating on cerebellar and cortical sensorimotor input [14]. In accordance with Rall's model [44] parietal cortex fibers may be assumed to establish synaptic contacts on more proximal parts of somatodendritic membrane of RN neurons than corticorubral axons of sensorimotor cortex.

Axon collateral branching of rubrospinal neurons

According to modern conceptions, RN participates in realization of dynamic control of movements by comparing and correcting the programmed and actual state of a peripheral apparatus. RN is the site of convergence of various loops operating between the spinal cord and the brainstem [24,29,38]. At the beginning of movements rubrospinal neurons are involved in the modification and perfection of a current motor activity. Such a role ascribed to RN cannot be realized without its numerous connections with many structures involved in realization of precise motor actions.

Morphological studies showed that there are RN projections to a number of nuclear structures in the brainstem [4]. RN projections to certain brainstem structures have been also shown electrophysiologically [10,45]. For that purpose the technique of antidromic impulses collision interaction has been used [51]. Axonal collaterals of rubrospinal neurons have been shown to project into the main sensory trigeminal nucleus, facial nerve nucleus, descending (inferior) vestibular nucleus, lateral reticular nucleus, external cuneate nucleus, gracile and main cuneate nuclei. Correlation between the antidromic impulse conduction time along the stem axon before and after collateral branching and the time of impulse conduction in the collateral themselves was analyzed. The number of axon collaterals of individual rubrospinal neurons to particular brainstem structures was studied. The tendency was observed of synchronous arrival of rubrospinal impulses to various brainstem centers, due to the increase in conductance velocity the further away these centers were from the RN [10,45].

The observed branching of axons of rubrospinal neurons in brainstem structures complements another important property of the main descending systems cortico-, rubro-, vestibulo- and reticulo-spinal: collateral branching of their axons to various level of spinal cord [1,41,46].

In phylogenetically older medial systems, reticulo- and vestibulo-spinal, greater amount of collaterals on the spinal cord level is revealed. In new lateral systems, cortico- and rubro-spinal, there are more collaterals on the brainstem level (in cortico-spinal one and on the thalamic level) [8]. Phylogenetically older systems must facilitate the control of activity aimed at coordination of movements of the fore and hind limbs as well as at the generalized regulation of muscular tonus. As opposed to them evolutionary younger systems are char-

acterized by greater participation in coordinating voluntary specialized movements.

The interaction of corticospinal and cortico-rubrospinal systems is realized on three brain levels: cerebral cortex, brainstem and spinal cord. In sensorimotor cortex corticospinal neurons inhibit neighboring corticorubral cells through recurrent axon collaterals. On the brainstem level large pyramidal neurons inhibit and small ones activate rubrospinal neurons. Corticorubral cells also cause activation in the latter. Corticospinal and corticorubral neurons, predominantly with slow conducting axons (5. 4-21. 6 m/sec) equally participate in excitatory corticofugal influences on rubrospinal neurons. Cortico- and rubrospinal cells produce a synergetic action on neurons of the spinal cord.

Powerful excitatory influences arrive to rubrospinal neurons from cerebellar structures. Their synaptic efficiency is high and they produce a large depolarizing tonic effect. In this respect RN first of all reflects cerebellar influences. There is a concurrent interaction between cortico- and rubrospinal systems presenting cortical and cerebellar control respectively.

Wide axon branching of rubrospinal neurons on the brainstem level emphasizes the importance of brainstem mechanisms in formation of a specialized motor action. Of the eight nuclear structures studied, in which the rubrospinal neurons' collaterals have been shown to exist, six are sensory relay nuclei. The direct connection of the latter with cerebellum has been shown. There is a powerful feedback system participating in the provision of a control over the influences which are realized by rubrospinal neurons. The mentioned system of feedback connections predominantly involves those cerebellar structures which in their turn control the activity of RN [10].

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ԿԵՂԵՎ-ԿԱՐՍԻՐ ԿՈՐԻՉ-ՈՂՆՈՒՂԵՂԱՅԻՆ ՀԱՄԱԿԱՐԳԻ ՆԵՅԲՈՆԱՅԻՆ ՄԵԽԱՆԻԶՄՆԵՐԸ

Վ.Բ. Ֆանարջյան

Կարմիր կորիզը (ԿԿ), ստորին ձիթապտուղն ու ուղեղիկը մասնակցում են շարժողական համաձայնեցման վրա թողած կորտիկոսպինալ եւ ռուբրոսպինալ վայրընթաց ազդեցությունների փոխարկումներում: Առնետների վրա գործիքային մշակումով ռեֆլեքսներում ռուբրոսպինալ ուղու միակողմանի ընդլայնական հատումը՝ ԿԿ եւ տեսաթմբի փորային կորիզի հետագա վնասումով, քերում է ավելի թույլ շարժողական եւ վարքային խանգարումների, քան ԿԿ կամ տեսաթմբի փորակողմային կորիզի նախապես մեկուսացված վնասումը: Ենթադրվում է, որ ռուբրոսպինալ ուղու նախնական ընդլայնական հատումը ծառայում է որպես ազդանշան կորտիկոսպինալ համակարգի հսկողության տակ կատարվող շարժողական գործունեության փոխարկման համար:

ԿԿ նեյրոնների վրա կատարված կորտիկոսպինալ եւ կորտիկոռուբրալ ազդակայնության փոխներգործության վերլուծությունը ցույց է տվել, որ դանդաղ հաղորդող կորտիկոսպինալ եւ կորտիկոռուբրալ նեյրոնները հավասար չափով մասնակցում են ԿԿ նեյրոններում ծագող դրդող հետսինապսային պոտենցիալներում:

ԿԼ նեյրոնների ակտիվության կեղևային եւ ուղեղիկային մոնոսինապսային հսկողությունը բնութագրվում է տարբեր արդյունավետությամբ: Կեղևային ազդակների մոդուլացնող ազդեցությունը գուցակցվում է հզոր ապարեւեռացնող ուղեղիկային էֆեկտի հետ:

Համաձայն գրական տվյալների, ինտերպոզիտոնորրալ սինապսներն ունեն գրգռի կայուն հաղորդման եզակի ունակություն: Սակայն մեր կողմից հայտնաբերվել են ինտերպոզիտոնորրալ սինապսներ, որոնք հաջորդական ազդակներ տալու դեպքում փոխում են գրգռն հաղորդելու ունակությունը:

Յույց է տրվել, որ ռուբրոսպինալ նեյրոնների արտոնների կողմնային ճյուղավորումները եւ նրանց պրոեկտումը դեպի ուղեղարնի տարբեր կառույցներ կարելու են մասնագիտացված շարժողական գործողությունների մեխանիզմների ձեւավորման համար:

Միաժամանակ հայտնաբերվել է հետադարձ կապերի հզոր համակարգի առկայություն, որը նպաստում է ուղեղային հսկողության ուժեղացմանը ռուբրոսպինալ համակարգի վրա:

НЕЙРОННЫЕ МЕХАНИЗМЫ КОРТИКО-РУБРОСПИНАЛЬНОЙ СИСТЕМЫ

В.В.Фанарджян

Красное ядро (КЯ), нижняя олива и мозжечок участвуют в переключении нисходящих кортикоспинальных и руброспинальных влияний на моторную деятельность. У крыс с выработанными инструментальными рефлексамы предварительная односторонняя поперечная перерезка руброспинального тракта с последующим повреждением КЯ и вентролатерального ядра таламуса приводит к более слабым моторным и поведенческим нарушениям, чем изолированное начальное повреждение КЯ или вентролатерального ядра таламуса. Предполагается, что предварительная поперечная перерезка руброспинального тракта служит сигналом для переключения двигательной деятельности под контроль кортикоспинальной системы.

Анализ взаимодействия кортикоспинальной и кортикорубральной импульсации на нейронах КЯ показал, что медленно проводящие кортикоспинальные и кортикорубральные нейроны в равной степени участвуют в возникновении возбуждающих постсинаптических потенциалов в нейронах КЯ.

Корковый и мозжечковый моносинаптический контроль активности нейронов КЯ характеризуется различной эффективностью. Модулирующее влияние корковых сигналов сочетается с мощным деполяризующим мозжечковым эффектом. Согласно данным литературы, интерпозиторубральные синапсы обладают уникальной способностью стабильной передачи возбуждения. Однако нами выявлены интерпозиторубральные синапсы, изменяющие свою способность к передаче возбуждения при нанесении последовательных сигналов.

Показано, что коллатеральное ветвление аксонов руброспинальных нейронов и их проецирование к различным структурам ствола мозга играют значительную роль в формировании механизмов специализирован-

ного двигательного акта. Наряду с этим установлено наличие мощной системы обратных связей, которые способствуют усилению мозжечкового контроля над руброспинальной системой.

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