Neurophysiology of gait for understanding basal ganglia motor disorders - from animal behaviors to the constructive approach -

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Abstract: We elucidated substrates for the execution of normal gait and to understand pathophysiological mechanisms of gait failure in basal ganglia dysfunctions. In Parkinson's disease, volitional and emotional expressions of movement processes are seriously affected in addition to the disturbance of automatic movement processes, such as adjustment of postural muscle tone and rhythmic limb movements during walking. These patients also suffer from muscle tone rigidity and postural instability, which may also cause reduced walking capabilities. Neurophysiological and clinical studies have suggested the importance of basal ganglia connections with the cerebral cortex and limbic system in the expression of volitional and emotional behaviors. Here we hypothesize a crucial role played by the basal ganglia-brainstem system in the integrative control of muscle tone and locomotion. The hypothetical model may provide a rational explanation for the role of the basal ganglia in the control of volitional and automatic aspects of movements. It can also be beneficial for understanding pathophysiological mechanisms of basal ganglia movement disorders. A part of this hypothesis has been supported by studies utilizing a constructive simulation engineering technique that clearly shows that an appropriate level of postural muscle tone and proper acquisition and utilization of sensory information are essential to maintain adaptable bodily functions for the full execution of bipedal gait.

Keywords: Basal ganglia-brainstem system, Postural muscle tone, Musculo-skeletal structures, Parkinson's disease

1. BASIC NEURAL STRUCTURES INVOLVED IN THE GAIT CONTROL

1.1 Contribution of forebrain structures

Activation of different areas in the forebrain evokes different types of goal directed behaviors. An important component of these behaviors is the locomotion, which has been considered as an emotional motor behavior that is triggered by signals from the limbic system to the brainstem [1]. However, accurate gait modification requires visuomotor processing in the cerebral cortex so that a precise foot placement can be achieved [2]. Prefrontal and premotor cortices (supplementary motor area and premotor area) are involved in motor planning and programming, respectively [3]. Motor programs at the premotor cortices may include those for postural control and precise limb movement control. Sensory information such as proprioceptive, vestibular and visual sensations is also required for planning and programming in addition to execution of locomotion [1]. The basal ganglia and the cerebellum can assist the above accurate cognitive operations by activating loops with prefrontal (cognitive loop) and premotor/primary motor (motor loop) cortices [4]. Loops involving the basal ganglia and the limbic system (limbic loop) contribute to emotional behavioral expression [1].

1.2 Mechanisms of integrating posture and locomotion by the brainstem and spinal cord

Regardless of whether the locomotion is emotional or volitional, it is accompanied by automatic processes that are controlled by the brainstem and spinal cord [1]. Basic structures involved in the control of locomotion and postural muscle tone are located in the midbrain [1]. One is midbrain locomotor region (MLR), and the other is muscle tone inhibitory region in the pedunculopontine tegmental nucleus (PPN). Signals arising from the MLR activate "muscle tone excitatory system" and "rhythm generating system". The excitatory system is composed of excitatory reticulospinal tract and monoaminergic pathways such as the coerulospinal and the raphespinal tracts. The excitatory reticulospinal tact and central pattern generators (CPGs), which are composed of spinal interneuronal networks, are major components of the rhythm generating system. Signals from the PPN excite "muscle tone inhibitory system", which is comprised of the pontomedullary reticulospinal tract and spinal inhibitory interneurons. This simultaneously inhibits α- and γ-motoneurons innervating extensor and flexor muscles and interneurons in transmission of reflex pathways (a part of them constitutes CPGs) so that it suppresses postural muscle tone and locomotion [8-10]. There are mutual inhibitory interactions between the excitatory and inhibitory system at the level of the brainstem and spinal cord. These systems contribute to the automatic processes of locomotion such as rhythmic limb movements and adjustment of muscle tone.

1.3 Gait control by the basal ganglia and pathophysiology of gait failure in Parkinson's disease

The brainstem receives excitatory inputs from the cerebral cortex and the limbic system, and inhibitory inputs from the basal ganglia [1]. The MLR/PPN area and the pontomedullary reticular formation receive inputs more preferentially from the premotor cortices rather than the primary motor cortex. Corticospinal system therefore controls precise limb-trunk movements and cortico-brainstem-spinal system may contribute to postural control that accompanies voluntary movement processes. It is established that basal ganglia control the activities of the cerebral cortex and the brainstem via ascending and descending projections. The former contributes to the planning, programming, and gait initiation via thalamocortical loops. The latter may

control gait initiation and modulate locomotor rhythm and postural muscle tone during locomotion.

In Parkinson's disease, loss of dopamine increases GABAergic inhibitory output from the basal ganglia [5]. Excessive inhibition upon thalamocortical loops may reduce cortical activities that enable planning, programing and sensory processing for execution of voluntary movements, resulting in hypokinesia and bradykinesia. An increase in the basal ganglia inhibition together with reduction of cortical excitation upon the MLR and the PPN may result in gait disturbance and hypertonus, respectively [6]. Consequently gait akinesia can be due to reduced activities of the cerebral cortex and the brainstem. Muscular rigidity is also involved in the gait akinesia because hypertonus or co-contraction of extensor and flexor muscles restricts trunk and limb joints' movements.

2. CONSTRUCTIVE APPROACHES TO BIPEDAL GAIT CONTROL

2.1 Design of bipedal simulation based on basal ganglia-brainstem system

Setting the appropriate level of postural muscle tone is necessary for execution of movements depending on environmental conditions [6] Bipedal walking requires alteration of body and leg movements in response to unpredictable perturbations so that stable posture during walking could be maintained. Tomita and Yano [7] proposed a new bipedal control system by modeling the basal ganglia-brainstem system and designed a bipedal robot, according to roles that were clarified by physiological studies [1, 6]. The ranges of motion of each joint are determined according to observed human data. Because adjustment of postural muscle tone is useful to determine body-leg synergies in response to changes in the environment, the robot has a postural muscle tone control system in addition to a locomotor executing system as gait control mechanisms. These two systems are integrated at the level of the spinal cord. During gait the subject receives proprioceptive information through their body and leg, mostly from the plantar foot, which has direct contact with the irregular ground. The ground reactive force exerted on the plantar foot was utilized to alter the level of postural muscle tone of body and leg and to maintain the body equilibrium. Visual sensation was also utilized to maintain postural equilibrium.

2.2 Role of postural muscle tone in the control of bipedal gait modification

Using this technique, examination was made to clear following two points. One was whether appropriate real-time regulation of postural muscle tone enabled the model to execute adaptable bipedal gait. The second was how changes in the operation of muscle tone control system modified bipedal gait. The simulation robot displayed flexible and robust bipedal gait that emerged from appropriate regulation of postural muscle tone in response to real-time alterations of the ground reaction force against various loads without explicit postural control. For example, when the robot was pushed or pulled forward or backward, it immediately adapted to the perturbation so that posture was steadily maintained. It is critically important to note that bipedal gait was greatly modified if postural muscle tone of the simulation robot was increased or decreased. In the case of hypertonus which was achieved by increasing the gain of stretch reflexes, walking speed reduced with a decrease in stride. The robot easily fell down if such perturbations were applied and the robust changes in postural control were ignored. Such gait disturbances are similar to those observed in Parkinsonian patients. Similarly, when postural muscle tone of the robot was reduced, it exhibited unstable bipedal gait characterized by agitation or postural sway of the trunk and a wide stance with postural instability. These characteristics resembled to the ataxic gait often observed in patients with a lesion in the medial cerebellum. Ground reactive force as a sensory feedback was not effectively utilized to control postural equilibrium when the level muscle tone of the model was either high (hypertonus) or low (hypotonus), indicating that the degree of real-time sensory acquisition depends on the level of muscle tone. These findings suggest that fine body structures as well as appropriate mechanisms of controlling muscle tone are essential to maintain stable postural and locomotor synergies in bipedal gait performance.

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