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Physiological Mechanisms and Movement Analysis in Parkinson's Disease

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Abstract

We present new ideas about motor control in the human central nervous system and about pathophysiological mechanisms of Parkinson's disease, and we describe the Posturo-Locomotion-Manual (PLM) method, which is a new technique utilizing optoelectronic camera recording for objective, fully quantitative, and standardized assessment of human motor performance. In the PLM test, recordings of body movements are made during a simple motor task, where the subject repeatedly moves a small object from its starting position on the floor to a shelf located at chin height a few steps forward. The duration of the postural (raising up), locomotor and the goal-directed manual phase of the forward directed body movement is automatically calculated by a small computer as well as the degree of coordination (simultaneity) of these phases. The technique has high resolution and has been used for clinical assessment of motor performance, drug testing, and so on, in neurological and geriatric practice.

Index Entries: Motor control; pathophysiology; Parkinson's disease; aging; motor performance; clinical assessment.

Introduction

Parkinsonian as well as other basal ganglia motor disorders have not previously been quantitatively analyzed in terms of movement pattern changes, because of the lack of adequate laboratory methods. The recent development of physiological concepts and new methods for movement analysis may give better conditions for pathophysiological interpretation and quantitative assessment of motor disorders. An understanding of motor control physiology is the basis for advancement in this field.

Phylogenetic Development of the Motor System

Comparative vertebrate physiology demonstrates a hierarchic organization of motor control with the output from low level motor pattern generators controlled and integrated at higher CNS levels for increasingly more elaborate performance in higher animals. Spinal and lower brain stem pattern generator nerve nets can produce the simple motor programs for such activities as swimming, gait, postural corrections, swallowing, and chewing when activated from centers in mesencephalon and pons—even in decerebrate animals. These brain stem centers are controlled from the basal ganglia and cortex. The pyramidal tract appears as a phylogenetic late invention for spatiovisually guided limb movements, projecting to basal ganglia and brainstem nerve nets, spinal pattern generators and motoneurons.

The simple motor program itself is viewed as a set of rules inherent in the pattern generator nerve net and expressed as preformed stereotyped movements. Behavioral efficacy and energy economy

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are important conditions for survival. Phylogenetic and ontogenetic development have generated mechanisms for smooth simultaneous and serial integration of simple motor programs to the higher level motor programs necessary for complex movements. A common characteristic of a preformed motor program is that it displays smoothly bell-shaped speed curves, giving optimal energy economy during the movement.

Control of Posture, Locomotion, and Goal-Directed Arm Movements

In our studies of human motor performance, we have focused on three basic motor abilities necessary for an independent life: the control of body posture, locomotion and manual dexterity.

Locomotion

Evidence that locomotor movements are governed from a spinal pattern generator comes from experimental work in both animals and humans. The segmental neuronal network of the swimming program pattern generator in a primitive fish, the lamprey, has been analyzed in detail, including its membrane properties, transmitters, receptors, and neuronal connections and the reticulospinal activating neurons *(1)*. The concept that locomotion pattern generators also exist in the mammal spinal cord has been supported by the finding that kittens, where the spinal cord was transected shortly after birth, developed almost normal hindleg gait patterns, adapting to increasing treadmill speed by changing the locomotion pattern, from gait to trot and gallop *(2)*. Locomotion patterns can also be induced in decerebrate cats *(3,4)* by chemical or electric stimulation in the mesencephalic reticular pedunculopontine nucleus and transformed into trot and gallop by increased stimulation. The spinal locomotor programs are controlled by GABA-ergic tonically active inhibitory neurons that project from the basal ganglia output nuclei, internal pallidum, and reticular nigral nucleus, to the mesencephalic locomotor regions *(5,6)*. Locomotor activation therefore presumes an active release or disinhibition.

The concept that the human bipedal heel gait represents an evolutionary transformation of the quadrupedal toe gait is strongly supported by the movement analysis of the primitive toe gait patterns in early childhood and its transformation during maturation and training to the adult upright bipedal heel gait *(7)*. Hypothetically the Parkinson shuffling toe gait may be regarded as a regression to the ontogenetically and phylogenetically more primitive toe gait program—a program disorder *(8)*.

Postural and Equilibrium Control

The idea that there exist specific programs used for postural control is supported by the experimental finding that electric stimulation in the ventral pons of decerebrate cats induced reflex standing by increase of extensor tone, whereas dorsal pontine activation reduced tone and caused a return to the prone position. In the intact cat, lying down, a continuous pontine electric stimulation successively induced uprising, standing, and start of walking *(9)*. In humans, the postural correction movements elicited by equilibrium perturbations have the character of preformed ankle synergies at weak and hip synergies at strong impacts, implying that stereotyped strategies or programs are recruited to preserve postural equilibrium *(10)*.

Reaching and Grasping

Forelimb reaching and grasping movements are organized by a nerve net of propriospinal neurons in cervical C3 and C4 segments in the cat and may be carried out even after lesions of the corticospinal and rubrospinal tracts with reticulospinal and tectospinal tracts left intact. They may even change direction of the reaching movement to a new target appearing during the movement visually guided by tectospinal pathways from the superior colliculi *(11)*. Human followup studies with the H-reflex technique demonstrated patterns of interneuron excitation and inhibition resembling the mechanisms demonstrated for integration in the C3-C4 system of the cat *(12,13)*.

Dual Control of Motor Programs

Locomotion, postural adaptation, and reaching and grasping behavior presumes that automated movement patterns can be adjusted to the visual and tactile information of environmental conditions, e.g., while running in terrain or climbing trees. It has been suggested that the evolution of corticospinal tracts is related to the increasing locomotor demands on the forelimbs of tree climbing animals and that the reaching and grasping originally developed for locomotion up the trees has

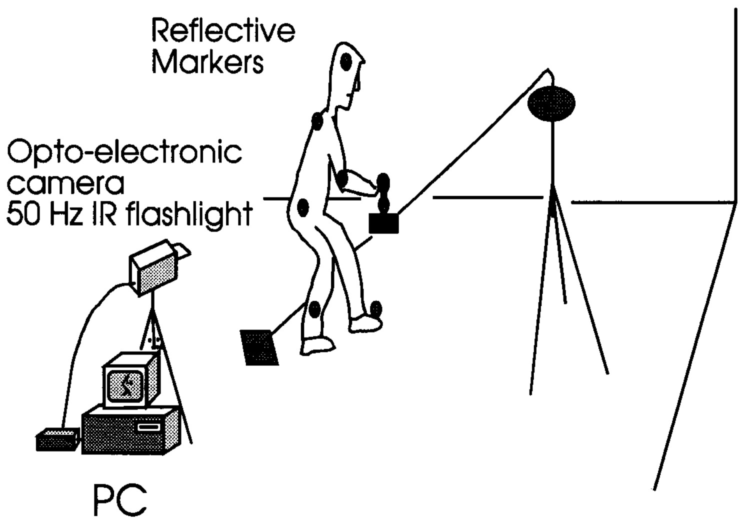

Fig. 1. The setup for movement analysis.

been the basis for the evolution of manipulative skills of the primate hand *(14)*. On this background the dual control of inherited motor programs may be conceived: The program pattern generators are driven and regulated from brainstem reticular premotor centers and precisely spatially adjusted to environmental conditions by direct corticofugal connections.

Basal Ganglia: Inhibition and Release of Motor Programs

Both experimental findings of compulsive locomotor hyperactivity after striatectomy *(15)* and demonstrations of degeneration of the enkephalin containing striatal spiny cells in the hyperkinetic form of Huntington's disease *(16)* strengthen the view that striatum exerts a general inhibitory influence on movements. Presuming intrinsically active motor program rhythm generators on a lower level in CNS, it is probable that an inhibitory descending control has a functional raison d'être and that the basal ganglia may select and prepare movement initiation by disinhibition (release) of motor programs. Using a technological metaphor, the basal ganglia may be regarded as the autopilot controlling on a subconscious level the coordination in a distributed computer system built up by different motor programs and by this activity giving the environmentally well informed pilot, the cortex, optimal conditions for integrating information and selecting the target for direct precise and well-prepared actions, undisturbed by a multitude of internal control functions.

Movement Analysis

Motor Program Deficiency in Parkinson's Disease

Using the optoelectronic camera to study how normal subjects pick up an object from the floor and move to position it on top of a stand a few meters ahead, we found that the path and movement trajectories for the object were almost straight lines, whereas those recorded from IR-light reflecting markers on different parts of the body were more complicated (Fig. 1). The velocity curves for the object and the body markers were, however, all of the "bell-shaped," "single shot" type. In contrast, recordings from parkinsonian patients showed irregular trajectories and multiple-phase velocity profiles *(17)*. We divided the movement into a postural (P) movement phase, depicting the changes in body attitude when the patient straightened out his or her body after bending down to pick up the object, a locomotion (L) phase, and a manual (M) phase, when the patient elevated his or her arm to place the object on the stand (Fig. 2A). This simple test movement, where the task was of a familiar everyday character, was called the Posturo-Locomotion-Manual (PLM) test, and used for clinical screening of different types of motor disturbance in Parkinson's disease *(18)* and also to analyze the changes of motor performance in normal subjects

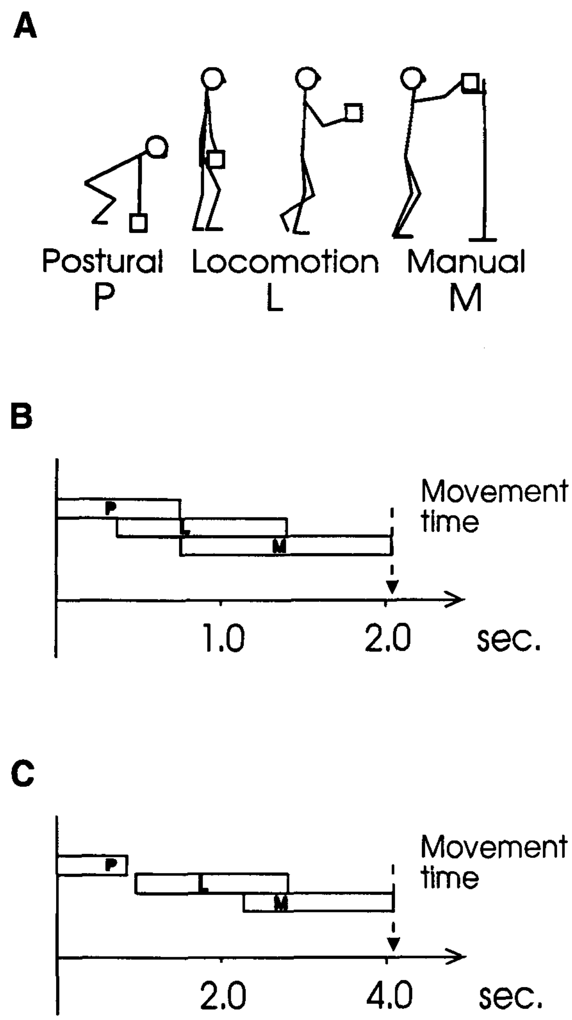

Fig. 2. The Posturo-Locomotion-Manual (PLM) test. **(A)** The patient repeatedly moves an object from the starting position on the floor to a stand, thereby forcing the body through postural movements, locomotor, and manual reaching movements. **(B)** The bar diagram depicts the duration of the P, L, and M phase, which normally are performed simultaneously. The movement time for the test is indicated by a dotted line. **(C)** In Parkinson's disease there is a loss of simultaneity in performance of the postural, locomotor, and manual part of the test movement. They are performed sequentially instead.

with advancing age *(19)*. We found that, typically, the performance of one or two of the PLM phases (e.g., the gait) was difficult for the Parkinson patient as reflected by its prolonged duration, whereas the other phases could be normal. This pattern of selective disturbance of the P, L, or M phase was found to be constant over time and could be evaluated in quantitative terms to form a PLM "symptom profile" characterizing the degree and type of motor disturbance in each patient *(18)*.

Motor Coordination in Parkinson's Disease and Old Age

Although the "profile" reflected insufficient control of the P, L, and M program generators, the degree of simultaneity with which these movement phases were carried out was thought to mark the coordinative capacity of the system, integrating postural, locomotor, and manual acts into a smooth compound movement. Normal subjects perform the test with a high degree of simultaneity (Fig. 2B), whereas Parkinson patients (Fig. 2C) often display low simultaneity or a disruption into a sequential performance *(20)*.

Conclusions

The concept of a hierarchical control of motor programs forms the base for our working hypothesis that the natural everyday act of lifting an object from the floor to a shelf on eye level some few steps away could be used as a test movement to analyze the integration of the individual motor programs for Locomotion, Postural regulation, and goal-directed Manual reaching movements into a higher order program, the PLM-test movement. We also assumed that this motor program coordination was a defect in Parkinson's disease.

When analyzing recordings of the PLM-movement it immediately turned out that the straight object trajectories and smooth speed curves found in the normal individual or after successful L-DOPA treatment were fragmented into individual uprising, gait, and arm elevation curves in patients with parkinsonism. Whereas in the normal individual gait started early in the uprising phase and arm elevation followed soon thereafter, with good simultaneous coordination between the different PLM phases, there was in Parkinson patients a change from simultaneous to serial organization of the PLM phases with increasing severity of disease. Increasing PLM-coordination difficulties has also been found in elderly normal individuals, particularly after 75 yr *(19)*. Although young individuals can increase their PLM simultaneity from deliberate to maximal speed more than twice as measured by a "simultaneity index," old people can improve the simultaneous coordination only marginally, presumably indicating less CNS processing power.

The optoelectronic camera system is a powerful tool for movement analysis, giving access to pathophysiological information in basal ganglia disease and a versatile tool for clinical documentation. It permits quantitative and qualitative studies of the performance of complex movements in freely moving subjects during purposeful acts of relevance for daily life. Today these systems are affordable and easy to use and in the clinical setting they can be operated by paramedical personnel. The PLM test is today a standardized test that can be used under normal hospital conditions in a variety of diseases and it provides truly objective and reproducible data. As an example, it has recently been used to evaluate the stabilizing effect of intraduodenal L-DOPA treatment on the "on-off" variations in Parkinson's disease *(21)*.

The optoelectronic movement analysis data thus gave supporting evidence for the hypothesis that the PLM-test permitted analysis of the coordination of low level motor programs into a high level program and that this coordination was disordered in Parkinson's disease.

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