Parkinson’s disease (PD) has been recognized as an idiopathic, degenerating disease presenting a mixture of a variety of different grades of rigidity, tremor, and akinesia. Today it is established that the axial pathology of the disease is the nigrostriatal DA deficiency, for which the treatment using levodopa or DA agonists produces markedly favourable results. Due to advances in drug treatment and resulting prolongation of the life span of PD patients, symptoms that had previously been not considered as being of core importance, have slowly become recognized as being important. These symptoms and difficulties in the later stage of the patients under long-term levodopa treatment for more than several years are disturbances of postural control and gait, emotional deterioration, and deterioration of cognitive function.

For understanding and treatment of a chronic and progressive disease like PD presenting a variety of symptoms, two investigative approaches are considered important. One is to elucidate the intracerebral pathophysiological mechanism underlying each of these symptoms such as rigidity, tremor, or akinesia. This avenue, which covers the anatomical, physiological, and biochemical investigations firstly based on neuropathological knowledge, is the classical one but is also today’s interest in the dynamic network within the basal ganglia. This will be described later by the author. The second approach, which has rapidly developed in recent years, is the investigation into the etiopathogenesis of the degenerative process specific for PD, i.e. into the nature of the slowly progressive neuronal death. This field may include the molecular biological investigation of the mechanism of more general cell death and genetic analysis.

§1. Back in May 1952 the author started the analytical approach by initiating stereotaxic pallidotomy for treatment of the rigidity and tremor of the disease, which surgery was later switched to thalamotomy. Microelectrode recording technique during surgical procedure was introduced in the author’s operation
theater as a routine method in 1972, and since then it has become possible to interpret the surgery-elicited changes in clinical symptoms in exact anatomical and physiological terms. Clinical effects on rigidity and tremor, the underlying pathophysiological mechanisms of these symptoms, and observations on the long-term postoperative follow-up study are described in the chapter, "Role of stereotaxic surgery in treatment of Parkinson's disease" in this book and in several other papers by the author (Narabayashi, 1990a).

Although the pace-maker of the tremor-generating mechanism is still not fully explained, pathological tremor, either parkinsonian or non-parkinsonian, is now almost completely alleviated by stereotaxic surgery on the Vim (ventral intermediate nucleus) of the thalamus without side effect. Tremor is interpreted as a circuit phenomenon based on both central and peripheral mechanisms with the Vim being a structure of key importance.

Rigidity is alleviated by lesioning of the VL (ventrolateral nucleus), the nucleus that lies just anterior to the Vim in the base of the thalamus and receives pallidal afferents. The pallido-VL-thalamic pathway is now considered responsible for producing rigidity and lies under the control of the nigrostriatal DA system.

§II. Akinesia is considered the most important core symptom of the disease, although the term itself has not been clearly defined and is used in a relatively vague manner. Akinesia is also analysed in the similar way and is classified into three subgroups. Type-I akinesia is slowness and unskillfulness of movement and is secondary to muscle rigidity, for it is almost completely abolished when rigidity has been removed by thalamic surgery. Type-II akinesia is also called primary akinesia; it is not related to rigidity but responds well to levodopa. Type III-akinesia seems more non-specific and is seen mostly in the chronic stage of the disease under long-term levodopa treatment, the symptoms of which have briefly been mentioned at the beginning of this chapter. Within the Type-III akinesia category, the symptom of "freezing" in gait and in repetitive movement is interested. It is frequently seen in longstanding PD cases and is difficult to control by levodopa. The underlying mechanism of gait-freezing was analysed by Inai, as will be described later in this chapter, by studying cases of "pure akinesia", which is the condition presenting the kinésie paradoxale type gait-freezing without any sign of rigidity and tremor and not responding to levodopa at all. Difficulty of rhythm formation over 2.5 hertz in repetitive movement in these patients was analysed as one of the underlying phenomena of freezing by Nakamura and Narabayashi (1976).

Gait freezing in the later stage of PD patients was hypothesized to be related to a central NE deficiency after the confirmation of lowered NE metabolism in the brains and CSF in the longstanding cases. L-threo-DOPS, the industrial precursor of NE, was introduced as an agent to compensate the metabolic deficiency and thus improve the symptom. Although it is a gentle drug with mild effect, it reverses clinical symptoms relatively well without any side effects. Details of L-threo-DOPS treatment are described in another chapter by Kondo.