CHAPTER V

DISCUSSION

Several studies showed that unilateral 6-OHDA injection to sN induced degeneration of the nigrostriatal DA system, produced an asymmetry in posture and movements (Sotelo et al., 1973 ; Robinson and Becker, 1983, Ziegler and Szechtman, 1990). The present study demonstrated that unilateral substantia nigra (SN) lesions by 6-OHDA induced ipsilateral turning behavior, postural asymmetry and abnormal resting EMG pattern. Similar lesions in the rats produced an asymmetric posture with the head and tail bent towards the side of the lesion (Ungerstedt and Arbuthnott, 1970 Ungerstedt et al., 1973 ; Siegfried and Bures, 1979). In the monkeys were injected 6-OHDA, they also developed the signs and symptoms of PD. They exhibited motor disorders in the form of an enchanced muscle tone, torticollis and circling around the body axis (Sambrook et al., 1979). The character of the enhanced muscle tone typical for extrapyramidal disturbances was confimed by EMG examination and expressed tonic activity continues of both soleus muscle, although it should also disappear in state at rest (Mempel and Wiezorek, 1990). The EMG finding in this experiment showed the continuous motor units activities at rest of involved leg but they were not seen in contralateral leg and in normal subjects. This is in good agreement with the EMG

findings that reported to produce rigidity of calf muscle at rest in rats (Steg, 1964). Addition to, Ungerstedt and his collaborators (1974) reported that the rigidity of the bilaterally 6-OHDA lesioned rats was easily evident in the EMG as a tonic motor unit discharge at rest. Moreover, clinical studies recordings of muscles contraction in the patient with unilateral (left) PD showed abnormal delay contraction of left quadriceps muscles (Wilson, 1925). These findings supported that a disinhibition of substantia nigra output neurons led to a muscular rigidity as showed an increased drive of both alpha- and gamma-motoneurons by reports of Thomus (1961) and Schultz (1984). Rigidity thus represents a positive symptom resulting from relase of other brain structures that are normally inhibited by SN. Based on the connectional anatomy and physiological studies of basal ganglia attempted to explain the neuropathological of PD. In figure 1, cortical afferents excited striatal neurons, which in turn inhibited the neurons of the pallidum and SN. The inhibition of the GABAergic and inhibitory output neurons of the basal ganglia resulted in increased activity by the thalamocortical neurons of the VA/VL/MD. DA was proposed to modify this circuit by inhibiting cholinergic striatal interneurons which normally excite striatal projection neurons. In PD, the absence of dopamine would leave the cholinergic interneurons driving the striatal projection neurons. This would eventually result in supranormal thalamocortical neuron activity (Albin et al., 1989). The latter was excessive and uncontrollable supraspinal drive to lower motoneurons, which was cause of rigidity in PD (Marsden, 1982).

This study investigated the importance of stimulus parameters on the EMG response, produced by cerebellar stimulation (CS). The results showed that the continuous resting EMG activity of triceps surae was suppressed by using stimulus frequencies 50 Hz and 100 Hz and duration 0.2 mS, (Figure.11). The current of stimulus frequency 100 Hz that was used to suppress the abnormal resting EMG activity of triceps surae was lesser than frequency 50 Hz. The effects of stimulus frequencies 50 Hz and 100 Hz have been reported to inhibit hypertonia and myotatic reflexes of decerebrate cats (Moruzzi, 1950). Similary to the reported by Sprague and Chambers (1954) that 50 Hz of cerebellar stimulation produced reciprocal postural muscle tone in decerebrated cat. Although the stimulus intensities for inhibition at 100 Hz was lower than the stimulus intensities at 50 Hz. In addition, stimulus frequency at 100 Hz of cerebellar cortex produced excitation of Purkinje cells that due to inhibition of hypertonia in decerebrated cat (Granit and Phillipp, 1957) and inhibition muscular hypertonus in monkey (Hemmy et al., 1977 ; Ebner et al., 1982) and man (Cooper et al., 1973). However, Upton and Cooper (1976) discussed that different effects of stimulus frequencies of cerebellar stimulation, might be attributed to species differences.

The present study showed that the effective stimulus duration was 0.2 mS, similar duration of cerebellar stimulation was used to decrease or reverse abnormal EMG pattern of stretch

reflex, and decrease torque that required to displace the arm of a spastic monkey (Ebner et al., 1980 ; 1982). The dependence of the suppression of EMG responses on the frequency of cerebellar stimulation was illustrated in figure 11 and 12, the duration was constant, 0.2 mS. Furthermore the frequency and duration stimuli used in this study are similar to those, used to reduce torque that required to displace the limb (Hemmy et al., 1977) and alternate the abnormal EMG pattern of stretch reflex in a spastic monkey (Ebner et al., 1980). It could be suggested that, application of these currents to the cerebellar surface might reduced cortical neuronal responsiveness, mediated via inhibition of the cerebellothalamo-cortical pathway, as shown in fig.19. In addition, other investigators found that 100 Hz of cerebellar stimulation was near optimal for reduction of amplitude of the somatosensory evoked potential (Sances et al., 1977/78).

In this experiment the suppressing EMG response of triceps surae appeared during the application of cerebellar stimulation on each area at different current intensities, while stimulus frequency was 100 Hz and duration was 0.2 mS. The importance of current intensity is illustrated in figure.9, 10, 13 and table3 for suppression of the abnormal resting EMG pattern. The results, however, showed that the abnormal resting EMG activity in triceps surae did not change, if current intensities were less than the thresholds. Stimulus thresholds of nine stimulated areas for this effect were up from 0.12 mA. The upper limit of stimulation reflected current intensities that required to produce

wild eyes and face expression or trembling. Also the highest current intensity, studied in this animal, limited at 1 mA. In the previous studies used different current intensities dependence on stimulus period (chornic or short time of stimulation), stimulus frequencies (high or low frequency) and animal (monkey) and man. The average threshold in previous study the current intensity stimuli was 1.5 mA, used in cerebral palsy with short period (10 min) of stimulation (Cooper et al., 1976). Nearly to the study of Davis and co-workers (1977/78) used stimulus intensities 0.3-1 mA at 150-200 Hz of cerebellar stimulation for controlled spasticity in cerebral palsy, Ebner et al., in 1982 used 2 - 3 mA at 100-300 Hz with stimulus duration 0.2 mS in monkeys, and Schulman et al., in 1987 used 1.4 mA at 150 Hz with short stimulation period (4 mins). Although, the high voltage or intensities, used usually in man, or with high frequency 200 Hz (Table. 1)

The effect of CS of previous studies have been investigated on non-specific area to change the abnormal EMG pattern. The present study investigated the specific area of the anterior cerebellar stimulation that suppress the abnormal resting EMG pattern of triceps surae. Stimulus threshold for this effect was different on each stimulated areas. The threshold of CS on the vermal part (C1, C2, C3) was higher than both intermediate parts of anterior cerebellar lobe. These findings of motor control of triceps surae were consistent with somatotopic mapping from Guyton (1991) which showed the topographic representation of hindlimbs lie in the intermediate zones.

The inhibitory effects have shown that the continuous motor units at rest of triceps surae disappeared during and after stimulation, not immediately. The effects of 40 sec of cerebellar stimulation on the anterior lobe were last for 20.8 sec to 1.33 min, approximately (shown in table 5). Such, these values were nearest to the early reported that the prolong effect of cerebellar stimulation on inhibition H reflexes in soleus muscle was 1 minute after cessation of stimulation in spastic patient (Cooper et al., 1977). The prolong effect might be produced by after discharge from the Purkinje units yielding inhibitory responses (Moruzzi, 1950). There was some doubt about the proportions of different types of neurons that were excited by stimulation of the cerebellar cortex. In addition to Purkinje cells, other neural elements such as climbing fibers, mossy fibers, granule cells and basket cells may be activated in the region of the stimulating electrodes. However, the current view was that efferent cerebellar outflow was entirely mediated by inhibitory Purkinje cells (Eccles et al., 1967). Neural stimulation is very crude in comparison with the complexity of the cerebellum, and one might speculated that frequent neural stimulation produced different patterns of reverberating neural circuits that interfered with fixation of the previous activity (Upton, 1978)

The prolong neurophysiological effects of stimulation may allow the use of maximum effective intervals between optimal epoche of stimulation, so that any cerebellar damage can be

minimized. Such cumulative effects may be attributable to direct effects of stimulation. The advantage of this effect may change background of EMG pattern of muscle to normal resting EMG pattern which express to the normal muscle tone. Then, the muscle could learn a new pattern of movement for generating of normal movement. Optimal this effects in physiological changes have seen excellent clinical results in the reducing of hypertonus in men (Upton and Cooper, 1976).

EMG studies were used to investigate the abnormal muscle tone which was produced by SN damage in this experiment. On basic of the motor unit reflects to the final common pathway for all nervous impluse controlling the muscle contraction (Tsementzis et al., 1980). The result of CNS disorder is the change of muscle tone which was investigated by EMG (Shaani and Wierzbicka, 1987) . The fact of EMG in normal muscle at rest is silent (Stolov, 1966). The continuous EMG activity at rest of triceps surae muscle was produced from releasing of activity in the corticospinal tract by SN dysfunction via cerebral cortex, which lead to enhance muscle tone at rest, called the "rigidity" (Thomus, 1961). The EMG data in this study showed that the continuous EMG activity of triceps surae was suppression by CS. Therefore, the effects of CS influence to inhibit and alternate the muscle rigidity to normal tone at rest.

One assumption for these effects was based on anatomical and electophysiological observation that the projection from the

cerebellar vermis exert inhibitory influences on the vestibular nuclei via fastigial nucleus (Carpenter, 1991). Since, stimulation of the anterior lobe of vermis of cerebellum produces a monosynaptic inhibition of neurons of the lateral vestibular nucleus which result in reduction of muscle tone. Other way, the ascending fastigial efferents that project to thalamic nuclei billaterally may be modified the excessive of cortical activity that was disinhibited from SN circuit. Moreover, the cerebellar intermediate parts have projections the inhibitory interneuron of thalamus to cerebral cortex via the interposted nuclei, as shown in figure 20. (Carpenter, 1991).

Such preliminary findings, reduction in amplitude of the thalamic component of auditory and somatosensory brain stem potentials, supported the hypothesis that there was likely to be inhibition of thalamic and cortical neurons after CS (Upton and Cooper, 1976). So, inhibition may well contribute to againt a background of descending facilitation from SN-lesioned. Whatever the mechanism of change the muscle tone was produced by cerebellalr stimulation, the beneficial effects were observed in EMG recording of more than thirty tree shews.

Summary, the results of continuous EMG activity of triceps surae muscle was produced by SN lesioned tree shrews. It was character of muscle rigidity that was returned to normal by stimulation of anterior cerebellar cortex with appropriate stimulus

parameters. Electrical stimulation at frequency 50 Hz and 100 Hz, duration 0.2 mS, on vermis and intermediate parts of cerebellar cortex produced the normal resting EMG activity in SN lesioned tree shrews. Stimulus current of the ipsilateral intermediate part of anterior cerebellar cortex was used lesser than the contralateral intermediate part and vermis for this effect. So, this study has also begun to indicate the complexities of muscle tone effects which can be evoked by cerebellar stimulation and investigated by EMG study. This finding may lead to understand the effects of cerebellar stimulation on EMG in Parkinsonian tree shrews and to modify the procedure to decrease rigidity in Parkinson's disease.

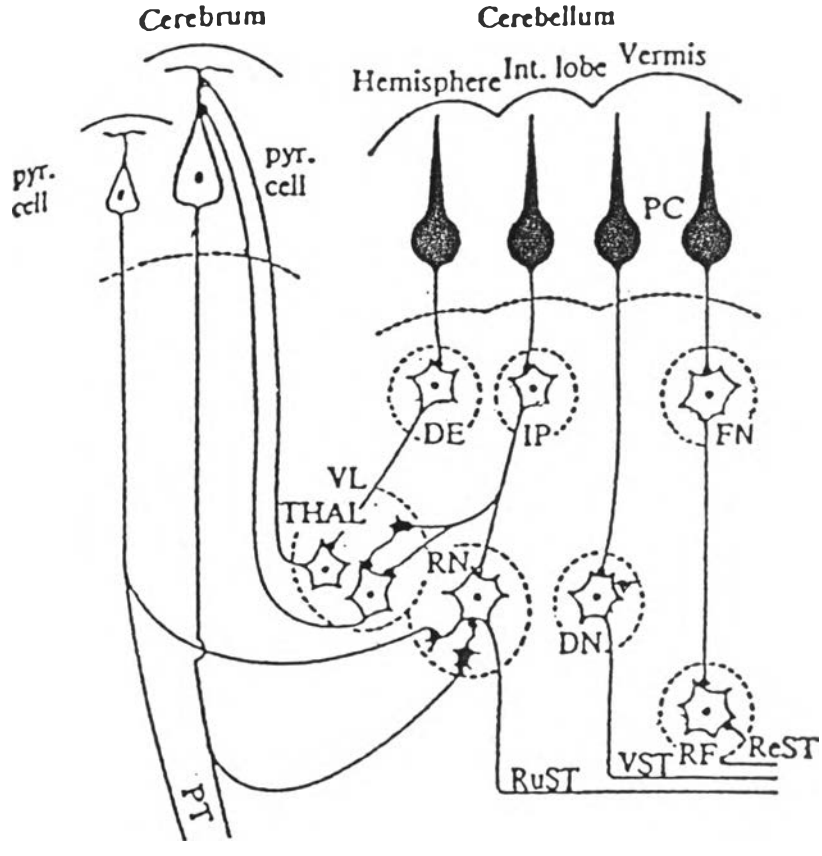

Figure 19. Various efferent pathways of Purkinje cells (PC) in the vermis, intermediate lobe, and hemisphere of the cerebellum. All inhibitory cells are shown in black. FN = fastigial nucleus ; IP = interpositus nucleus ; DE = dentate nucleus ; RF = reticular formation ; DN = Deiters' nucleus ; RN = red nucleus ; VL THAL = ventrolateral nucleus of thalamus ; PYR = pyramidal cell ; ReST = reticulospinal tract ; VST = vestibulospinal tract ; RuST = rubrospinal tract. The pathways are shown from pyramidal cells to the VL thalamus and red mucleus. (From Eccles, The Dynamic Loop Hypothesis of Movement Control, Information Processing in the Nervous System. New York : Springer Verlag, 1969. p.255.)

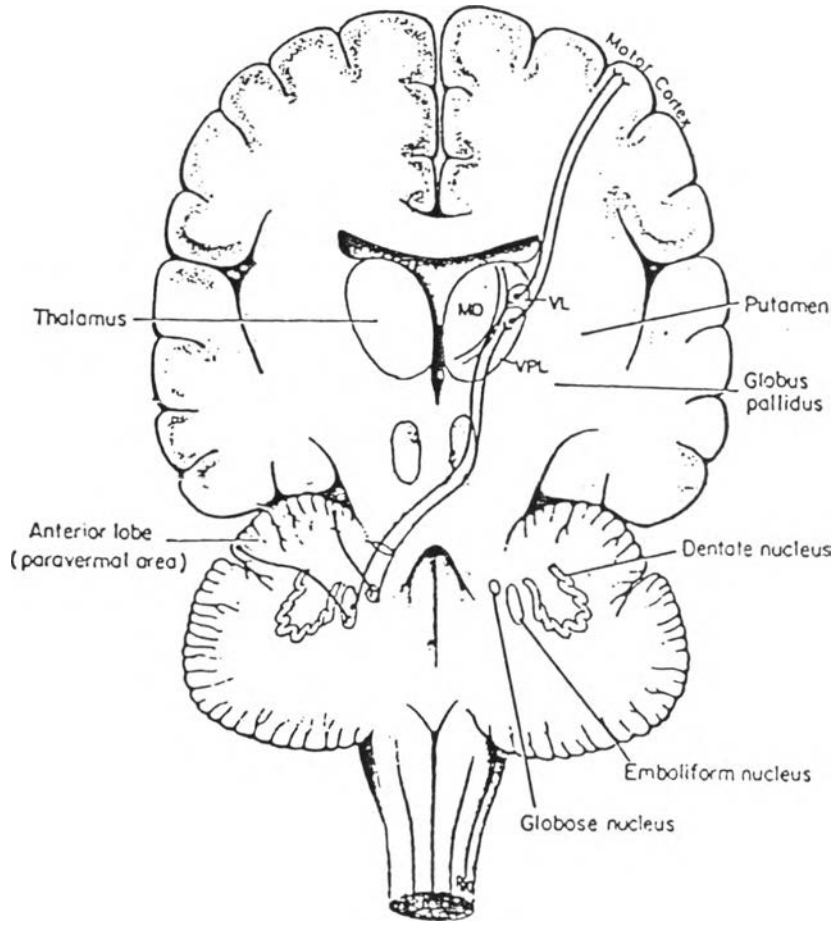

Figure 20. Schematic diagram of the projections from the interposed nuclei of the cerebellum (i.e., emboliform and globuse nuclei) via the superior cerebellar peduncle. The interposed nuclei receive afferents from the paravermal cortex. Thalamic projections from the interposed nuclei terminate in the cell sparse zone of the thalamus (VL and VPL). And thalamic neurons receiving input from the interposed nuclei project to the primary motor cortex. (From Carpenter, Core text of Neuroanatomy, 1991 ; courtesy of Williams & Wilkins, 1991. p.241.)