CHAPTER II

BACKGROUND INFORMATION

The cerebellum, along with the midbrain, and the corticospinal tracts, is one of several components of the central nervous systems (CNS) that regulates muscle spindle activities (Lechtenberg, 1993). Electrical stimulation of the cerebellar cortex was initiated in 1972 as a mean of prosthetically mobilizing the inhibitory potential of Purkinje cell efflux in various neurologic diseases (Cooper, 1973; Cooper et al., 1973). The development of this concept evolved from the well-documented fact that the cerebellum is intimately involved in complex mechanisms which control somatic muscle length and tone (Cooper et al., 1976 ; Ebner et al.,1980 ; Schulman et al., 1987), gait (Hershler et al., 1989), posture (Sprague and Chambers, 1954), and initiation cortical input and output signals (Doudet et al., 1990).

The prior classical experiments by Lowenthal and Horsley in 1897 demonstrated the fact that stimulation of anterior cerebellum inhibited extensor hypertonus in decerebrated cat. Other experimental investigations have shown that the stimulation in the same area decrease epileptic activities

in cat, monkey and man (Cooper et al., 1973 ; Bantli et al., 1976 ; Hemmy et al., 1977). The mechanism underlied these phenomenon was posturated by the fact that cerebellar stimulation would stimulate a great number of Purkinje cell. These cells would inhibit cortical activity through the ascending reticular formation and the non-specific thalamic nuclei (Bantli et al., 1976). Upton and Cooper (1976) found that the anterior cerebellar stimulation played major role controlling the excitability of alpha motoneurons via thalamus which relay to cortical motor area. The thalamus has been demonstrated as ventrolateral (VL) thalamic portion by Massion and Rispal-Padal (1972). The signal from Purkinje cell after cerebellar stimulation would mediated through this relay centre to the parts of motor areas 4 and 6 which control limb and axial muscles (Massion and Rispal-Padal, 1972).

Moreover, the studies in monkeys showed that the ipsilateral anterior lobe and bilateral intermediate lobe of cerebellum control hindlimb muscular movement (Harvey et al., 1979 ; Brodal, 1981). In addition the intermediate part of cerebellar cortex has connection to interpositus nuclei that control proximal and distal muscles of limbs while the vermis part has connection to fastigial nucleus that control proximal and axial muscles (Mani et al., 1964 ; Chambers and Sprague, 1955).

The effects of cerebellar stimulation have been reported to relief of hypertonia, movement disorders and epileptic activities in

a large number of patients (Cooper et al., 1973 ; 1976 ; Wood et al., 1976 ; Davis et al., 1977/78 ; Fishers and Penn, 1978 ; Whittaker, 1980 ; Schulman et al., 1987 ; Hershler et al., 1989). There are numerous previous experiments demonstrating effect of cerebellar stimulation on muscular activites in cats (Moruzzi, 1950 ; Sprague and Chambers, 1954 ; Granit and Philipp, 1957 ; Llinas, 1964), monkeys (Hemmy et al., 1977 ; Ebner et al., 1980 ; 1982) and men (Cooper, 1973 ; Cooper et al., 1976 ; Davis et al., 1977/78 ; Mclellan et al., 1978 ; Penn et al., 1978 ; Fisher and Penn, 1978 ; Upton, 1978 ; Whittaker, 1980, Ebner et al., 1980 ; 1982 ; Davis et al., 1987 ; Schulman et al., 1987 ; Hershler et al., 1989), as shown in table 1.

Ebner and co-workers (1980) reported the reductions in tonic and reflexly evoked electromyogram(EMG) activity of biceps and triceps brachii muscles as well as reductions in torque about 50% by stimulation of cerebellar cortex in spastic primates. Extremely important is the observation that cerebellar stimulation can decrease the exaggerated muscular tone which investigated by the EMG study (Ebner et al., 1980 ; 1982). In addition the effects of cerebellar stimulation are able to modify the excitability of segmental motoneurone pools (Fisher and Penn, 1978). These findings show that the cerebellum could effect the muscle tone.

Since the effects of cerebellar stimulation are complex, involving not only physiological but also anatomical connection. The ultimate concept is the summation of these effects on integrated performance in a severely damaged motor system. Possibly that cerebellar stimulation exerts its most significant therapeutic effect neither in "correcting" motor system abnormalities or in "producing a better balance" between damaged and relatively undamaged motor subsystems (Fisher and Penn, 1978 ; Ebner et al., 1980).

It is interesting that the function of the basal ganglia, like the cerebellum, are drived on motoneurons pool via thalamus, midbrain and cerebral cortex, as well as regulated the muscular tone (Delong, 1990). In many studies, the basal ganglia diseases produced abnormal movements and disturbance of muscular tone (Schultz, 1984 ; Watts et al.,1991), by a mechanism known as the "release phenomenon" (Chusid,1985).

The most common of basal ganglia diseases is Parkinsonism or Parkinson's disease (PD) that presented to expression of rigidity (Denny - Brown, 1960). Parkinson rigidity may well result primarily from a lack of modulation of cortical motor output due to a disturbed inhibitory feedback from the basal ganglia (Burke et al., 1977). These clinical rigidity are reflected in the EMG findings and in passive tension (Rushworth, 1960). But in the resulting hypertonicity, there appears to be

no evidence of primary defect in the fusimotor system (Burke et al., 1977).

The classical normal muscle tension is defined as the tonus in the muscle when it is elongated passively. Muscle tone can be directly measured by passive movement of limb (Duggan and Melellan, 1973) and indirectly measured by EMG activities based on the principle that increased muscle contraction is associated with increased electrical activity under physiological condition (Herman, 1970). EMG activity produced by skeletal muscle has been found useful in investigation and understanding of a variety of neurologic disorders with changes in muscle tone (Shahani and Wierzbicka, 1987). Because the motor unit reflects to the final common pathway for all nervous impulses controlling the skeletal muscle. Disorders of the CNS should result in abnormalities of EMG (Tsementzis et al., 1980). In generalisation, EMG techniques that have been used for the study of normal (Clemmesen, 1951) and abnormal motor control (Gunieben and Schulte-Matter, 1992), and the treatment of patients with disorders of motor control (Thilmann et al.,1991). Electrical silence in normal human muscle at rest is a basic fact of EMG study (Stolov, 1966).

The muscle tone of rigidity is static, the resistance to stretch is present at all speeds of stretch (Burke et al.,

1977). This character is the cogwheel phenomenon (Delwaide et al., 1986). Thirteen of 16 Parkinonian patients, reported by Berardelli and co-workers (1983) showed that an increase of baseline EMG activities when they were at rest contained more spontaneous muscle spindle activity than relaxed normal subjects. These resting EMG findings were found in the calf muscle of rigid-rat (Steg, 1964), in the biceps and triceps brachii muscles of monkeys with substantia nigra lesioned (Doudet et al., 1990),and in the soleus muscles of cats that were injected 6-hydroxydopamine (6-OHDA) (Mempel and Weiczorek, 1990). The increased muscular tone at rest reflects increased alpha motoneuronal drive. However, Thomas (1961) and Marsden (1982) attributed to exaggeration of the resting muscle tone that resulted in the major excitatory drive on the motoneurones which is transmitted not over segmental stretch reflex pathways but by descending from higher motor centers.

The development of animal models became a great help in studying some basic pathophysiological and electrophysio-logical findings of Parkinsonism, including an enhanced muscle tone that called rigidity(Schultz, 1984 ; Ohye, 1987 : Rivest et al., 1991). Animals with the lesion of the substantia nigra as a resulted of 6-OHDA caused a fall in the dopamine level of striatum (Iversen, 1973 ; Ungerstedt et al., 1973). This reduction correlates with that seen in Parkinson's disease where clinical symptoms appear only after a dopamine reduction of about 60 - 80 % (Scherman et al., 1989). In monkeys profound nigrostriatal

damage result in bradykinesia with an enhanced muscle tone, torticolis, circling around the body axis and postural asymmetry (Sambrook et al., 1979).

DA was proposed to modify basal ganglia circuit by inhibiting cholinergic striatal (caudate nucleus and putamen) interneurons which normally excite striatal project neurons (Racagni et al., 1978), as illustrated in figure 1. Consequently, the activity of the SN can thus modulate the basal ganglia circuit either at the level of the striatum or in the thalamus. In addition, substantia nigra lesion have been thought to have a releasing of activity in the corticospinal tract, which then produced facilitating effect on the interneuronal mechanisms of the spinal cord and lead to excessive impulse-firing to the muscle (Thomas, 1961). The cortex is modulated by the thalamus, which in turn receives input from the basal ganglia, sensory systems and the cerebellum. And the cortex can modulate these structures and sends descending tracts to brainstem motor nuclei and to motoneurons (Albin et al., 1989).

It seems that in the operative treatment of rigidity, the procedure of choice is the interruption of the pallido-thalamo-cortical system before it reaches the cortex, from which point it would project via efferent pyramidal and extrapyramidal connection to the anterior horn cells, causing excessive discharges. The interruption of this pathway abolishes the

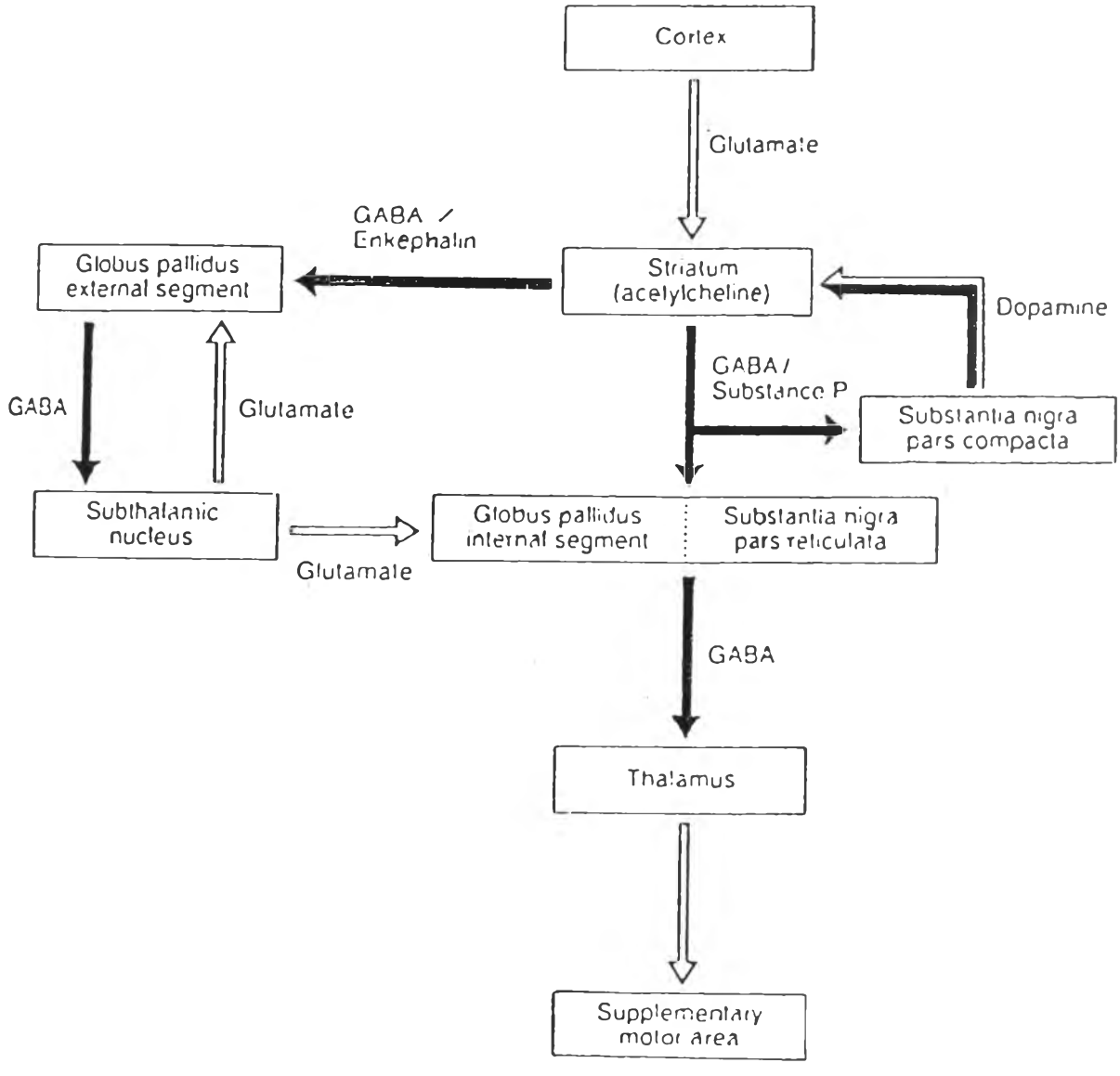

Figure 1. Schematic diagram of the basal ganglia pathways. Arrowheads indicate the direction of impluse flow. (Black arrows represent inhibitory pathways ; white arrows represent excitatory projections.) (From Kandel et al., Principles of Neural Science, 1991. p.653.)

fascilitatory influences on the interneuronal-anterior horn cell mechanism, resulting in suppression of the enhanced myotatic reflexes , and it also suppresses descending impulses generating resting rigidity (Thomas, 1961).

From the previous studies which was reported that the electrical stimulation of the cerebellar cortex caused the mobilizing the inhibitory potential of Purkinje cell efflux in various neurologic syndromes, such as spasticity, that appear to be a result of disinhibition of motor or behavioral activity. There fore, the present study was designed to observe the effect of electrical stimulation of the anterior-lobe of cerebellar surface in substantia nigra lesioned animal model from triceps surae by EMG investigation. The hypothesis was based on anatomical and electrophysiological studies of cerebellocortical loop in cats and primates. If the cerebellar stimulation changed the excitability of cerebellar nuclei projecting to the thalamus that could result in changing of cortical excitability in turn which might modify or suppress the descending impluses generating resting rigidity. Furthermore, this work defined the optimal stimulus parameters (i.e., frequency, duration and current intensity) and areas of the anterior cerebellar stimulation which could suppress the abnormal EMG pattern of triceps surae at rest in tree shrews with substantia nigra lesioned.

Table 1 Summary of experimental of cerebellar stimulation

Year	Reference	Subjects	Stimulus parameters	Effects of cerebellar stimulation
1950	Moruzzi	cats	50,100 and 300 Hz 1 mS > 6 volts	: inhibited hypertonia and myotatic reflexes of decebrate cats
1954	Sprague and Chambers	cats	50 Hz 0.1 mS 1-13 days	: reciprocal postural muscle tone
1957	Granit and Phillipp	cats	100 Hz 5.5 mS < 1 volt	: excited Purkinje cells due to inhibition of decerebrated rigidity (used the strain-gauge myograph)
1964	Llinas	cats		: inhibited decerebrated rigidity

Year	Reference	Subjects	Stimulus parameters	Effects of cerebellar stimulation
1973	Cooper	man	: 200 Hz 10 Volts : 10 HZ 10 volts	: decreased ipsilateral rigidity and spasticity : ameliorated convulsion
1973	Cooper, et al	man	: 100-200 Hz 1 mS 14 volts 2 - 4 hours : 10 Hz	: inhibited muscular hypertonus : inhibited the seizures
1976	Bantli, et al	cats	100-200 Hz 0.1 mS	: influenced processing of ascending sensory information

Year	Reference	Subjects	Stimulus parameters	Effects of cerebellar stimulation
1976	Copper, et al	cerebral palsy	200 Hz 1.5 mA 10 mins	: improved in spasticity as well as athetosis, speech, gait, deep tendon reflex, ADL , and improved in psychometric test scores
1977	Wood, et al	man	200 Hz 1 mS 3-12 mA	: increased in CSF norepinephrine
1977	Hemmy, et al	monkeys	100 Hz 0.25 mS 10 mA 6 mins	: reduced spasticity and cortical neuronal responsiveness
1978	Mclellan, et al	man	200 Hz 0.5 mS 12-14 mA	: improved spasticity

Year	Reference	Subjects	Stimulus parameters	Effects of cerebellar stimulation
1978	Ratusnik, et al	cerebral palsy	no data	: impoved speech characteristics
1978	Fisher and Penn	man	100 Hz 0.5 mS	: decreased in motoneurone pool excitability or normalisation of the relationship between flexor and extensor motor neurone pools that could affected tone
1978	Penn, et al	cerebral palsy	20-30 Hz and 200 Hz 0.5 mS 6-20 mA	: reduced rigidity and coactivation of muscles (measured compliance and EMG of anterior tibial and gastrosoleus muscles)

Year	Reference	Subjects	Stimulus parameters	Effects of cerebellar stimulation
1977/78	Davis, et al	cerebral palsy	150-200 Hz 0.5 mS 0.3-1 mA	: controlled spasticity and involuntary movements ; improved voluntary movements associated with feeding, dressing and ambulation with walker
1978	Upton	man	200-300 Hz 0.5 mS 2 volts	: relieved spasticity
1980	Whiltaker	man	100 Hz 250 mS 6-8 volts	: did no harm

Year	Reference	Subjects	Stimulus parameters	Effects of cerebellar stimulation
1980	Ebner, et al	monkeys	200 Hz 0.2 mS 3.6 mC/cm^2 10 - 30 mins	: decreased or reversed abnormal reflex patterns (EMG) with decreased torque that required to displace the limb
1982	Ebner, et al	monkeys	100-300 Hz 0.2 mS 2 - 3 mA 10 - 30 mins	: modified the organization of the segmental reflexes : produced normal reciprocal relationship of the EMG activity of the triceps and biceps muscle

Year	Reference	Subjects	Stimulus parameters	Effects of cerebellar stimulation
1987	Davis, et al	man	no data	: 66 % improved motor performance testing and 15 % improved mood states (tension, depression, anger, fatigue, confusion)
1987	Schulman, et al	cerebral palsy	150 Hz 0.5 mS 1.4 mA 4 mins	: improved in range of motion of joints and in motor ability (Double blind study)
1989	Hershler, et al	cerebral palsy (adult)	200 Hz 16-40 volts 25 mins	: improved gait and speech