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Thalamic Deep Brain Stimulation for Parkinson's Disease

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1. Introduction

With recent advances in neuroimaging and neurosurgical techniques as well as better understanding of functional motor brain circuits, there is increasing evidence that electrical deep brain stimulation (DBS) can be a powerful and safe therapeutic option for medically intractable movement disorders and neuropsychiatric diseases. For more than half a century, the ventrolateral (VL) nucleus of the thalamus has been an anatomical target for stereotactic surgeries (e.g., ablation surgery and DBS) treating various types of tremors, including Parkinson's disease (PD)-associated tremor. The VL nucleus comprises the nucleus ventralis intermedius (Vim) and the nucleus ventralis oralis (Vo) (Hassler, 1959). Currently, thalamic DBS is widely used because of its reversibility, adjustability, and low level of invasiveness. Thalamic DBS of the Vim nucleus can effectively alleviate parkinsonian tremor; however, it does not provide consistent improvement in parkinsonian symptoms other than tremor. Therefore, its use is limited to patients with tremor-predominant PD, in whom other motor symptoms are not disabling. In this review, we will survey the rationale and current use of thalamic DBS in the treatment of PD.

2. Functional anatomy of the VL thalamic nucleus

The VL thalamic nucleus is a major target for DBS in the treatment of movement disorders. With respect to therapy targeting PD, the Vim nucleus is frequently the site for the treatment of medically intractable tremor. The anatomy and function of the fiber connections of the Vim nucleus (Fig. 1) are important in considering the therapeutic and adverse effects of this surgery. We first present a brief review of anatomical studies based on primate studies of the VL thalamic nucleus.

Cortico-thalamo-basal ganglia loops are suggested to have specialized functions corresponding to the cortical areas participating in each loop (Alexander & Crutcher, 1990). Reciprocal thalamo-cortical connections play a role in maintaining these parallel processing loops. Functionally segregated parallel loops may be integrated via non-reciprocal fiber

connections between the thalamus and cortex, terminating in the superficial and deep cortical layers. These terminals could influence various cortical areas that, in turn, project toward the striatum, which sends efferents back to the thalamus. In addition, non-reciprocal corticothalamic projections terminate in thalamic regions that participate in other processing loops (McFarland & Haber, 2002). As a thalamic-level constituent of the motor loop, the VL nucleus mediates movement-related processing.
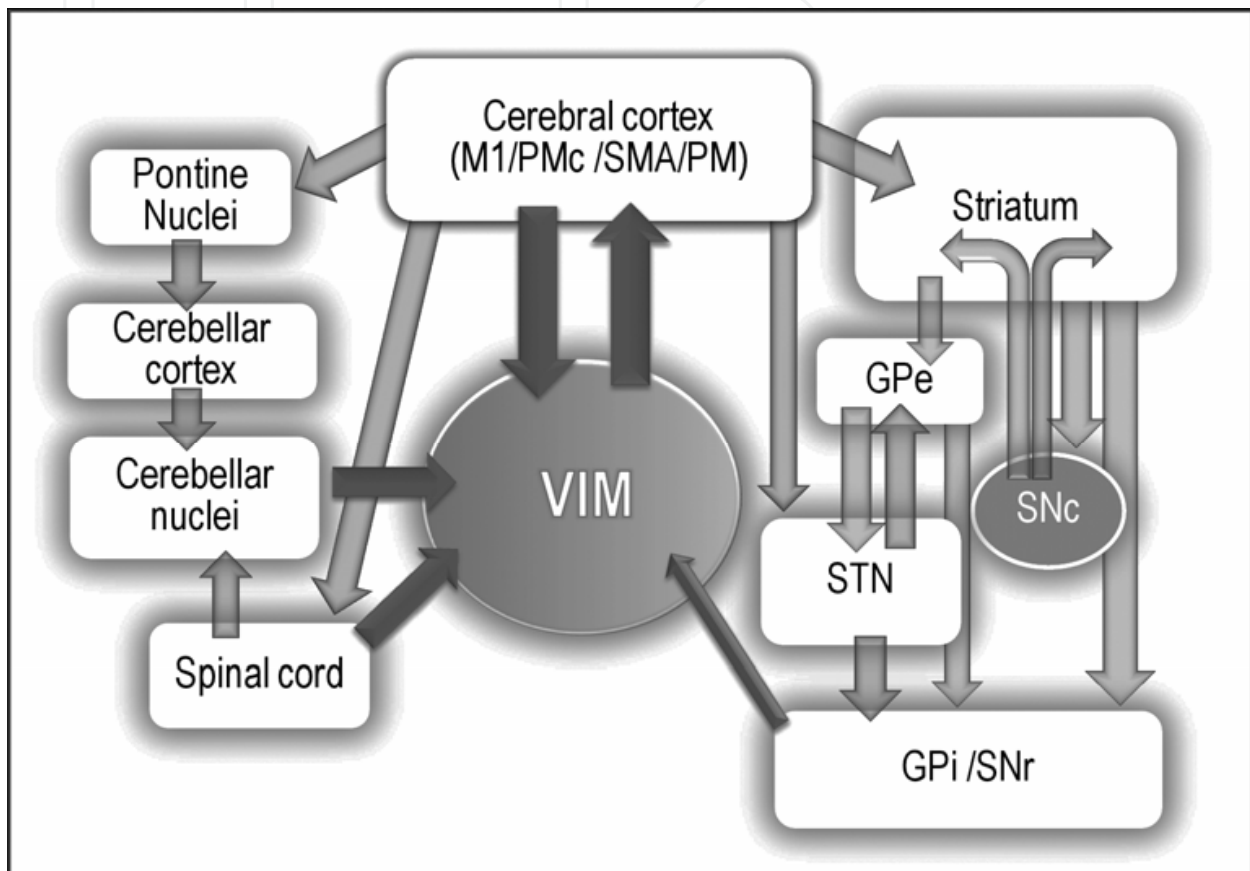

Fig. 1. Major fiber connections of the Vim nucleus in the movement disorders. Abbreviations: PMc, primary motor cortex; SMA, supplementary motor area; PM, premotor cortex; GPe, globus pallidus externa, STN, subthalamic nucleus; GPi, globus pallidus internus; SNr, substantia nigra pars reticulate; SNc, substantia nigra pars compacta.

The VL thalamic nucleus comprises 2 major functional territories (Asanuma et al., 1983a; Kultas-Ilinsky & Ilinski, 1991; Ilinsky & Kultas-Ilinsky, 2002). The cerebellothalamic excitatory afferents terminate predominantly in the contralateral Vim nucleus, creating a posterior-to-anterior gradient of terminal densities through the VL nucleus. In contrast, the pallidothalamic inhibitory afferents terminate preferentially in the ipsilateral Vo nucleus, with an anterior-to-posterior gradient of terminal densities through the VL nucleus (Percheron et al., 1996; Sakai et al., 1996; Gallay et al., 2008). These 2 functional territories thus receive different afferents that interlace and, at least in part, overlap (Rouiller et al., 1994; Sakai et al., 1996). A somatotopic arrangement, i.e., a medial-to-lateral distribution of facial-, forelimb-, and hindlimb-receptive fields, also exists in VL thalamic nucleus (Strick, 1976; Asanuma et al., 1983b; Vitek et al., 1994, 1996; Ohye, 1997). These findings indicate that

the Vim and Vo nuclei receive differentially weighted pallidal and cerebellar afferent inputs (Sakai et al., 1996; Gallay et al., 2008) and suggest that they might, at least in part, integrate these inputs in a somatotopic fashion (Sakai et al., 1996). Given that spinothalamic afferents terminate in the posteroventral part of the VL nucleus along a posterior-to-anterior gradient, Craig (2008) suggests that this part of the nucleus is not simply a relay of primary cerebellothalamic inputs, but rather, represents the convergence of the spinothalamic and cerebellothalamic movement-related pathways.

Neurons of the VL nucleus project to the sensorimotor territory of the striatum, preferentially as collaterals of thalamocortical projections via multisynaptic connectivity. Convergence of the thalamic and cortical inputs could occur in this striatal region (McFarland & Haber, 2000, 2001). In a monkey model of PD, corticostriatal and thalamostriatal synapses in the sensorimotor striatum show complex ultrastructural remodeling that might increase synaptic plasticity (Villalba & Smith, 2011). Thus, ventral thalamic motor nuclei might act not only as relay nuclei but also as highly ordered nuclei providing positive feedback to the sensorimotor striatum (Smith et al., 2004) and thus sustaining disinhibition of specific thalamocortical circuits until their goals are achieved. Alternatively, these nuclei might reinforce or facilitate selective basal ganglia circuits, thereby suppressing unwanted movements (McFarland & Haber, 2000).

The thalamic territory innervated by cerebellar afferents sends efferents predominantly to the primary, pre-, and pre-supplementary motor cortices, while the thalamic territory innervated by pallidal afferents sends efferents predominantly to the primary and premotor cortices (Rouiller et al., 1994; Sakai et al., 2002; Morel et al., 2005). This divergence and convergence of projections from pallidal and cerebellar afferent-receiving thalamic areas across multiple areas of motor and premotor cortex is now well accepted (Morel et al., 2005). These pathways seem to directly participate in modulating the nature of motor-related information.

Local GABAergic inhibitory interneurons in the thalamic nuclei receive cerebellar, pallidal, and cortical afferents, and constitute complicated inhibitory and excitatory influences upon thalamocortical projection neurons. The thalamic reticular nucleus also receives excitatory collateral inputs from corticothalamic projections and, in turn, provides inhibitory and excitatory outputs to the thalamocortical projection neurons. The so-called "burst" and "tonic" modes of activity have been observed in thalamic neurons. In the "burst" mode, the transfer of information has a high signal-to-noise ratio that is conveyed in a non-linear manner such that new signals are readily identifiable but not readily analyzed. In the "tonic" mode, there is a linear transfer of the activity of specific afferents, but the signal-to-noise ratio is low (Godwin et al., 1996). Similar patterns of activity have been seen in the lateral thalamus (Tsoukatos et al., 1997; Zirh et al., 1998). The thalamocortical projection plays an important role in the preparation for, and initiation and execution of, the movements in the motor thalamus (Kurata, 2005). Electrical stimulation of corticothalamic fibers causes the thalamic relay neurons to change from "burst" to "tonic" mode (McCormick & Von Krosigk, 1992; Godwin et al., 1996). This switch in the firing patterns of thalamocortical fibers could be mediated by the corticothalamic feedback pathway via reticular neurons (Sherman & Guillery, 2006). Thus, local thalamic circuitry may involve scaling of neural processing, especially by increasing the temporal resolution of afferent information. In addition, these local inhibitory neurons are required for network synchronization (Huguenard, 1999).

3. Pathophysiology of parkinsonian tremor

Accumulating evidence suggests that among parkinsonian symptoms, akinesia/rigidity and tremor may be associated with functional impairments of different motor circuits. It is generally thought that tremor is primarily related to the cerebello-thalamo-cortical pathway, while akinesia/rigidity is rooted in the basal ganglia-thalamo-cortical pathway. Recent results from clinicopathological, electrophysiological, and neuroimaging studies on PD patients are discussed in the following sections.

3.1 Clinicopathological studies

A statistical analysis performed using the Unified Parkinson's Disease Rating Scale (UPDRS) showed that the motor score for tremor is independent of the scores for other motor symptoms in PD patients (Stochl et al., 2008). It was also noted that severity of tremor does not correlate with severity of dopamine loss or clinical disease progression (Zaidel et al., 2009). Rajput et al. (2009) reported that tremor-dominant PD patients showed slower disease progression and less dementia than did akinesia/rigidity-dominant PD patients. A postmortem histopathological study showed that dopaminergic cells in the midbrain retrorubral area, which project to the dorsolateral striatum and ventromedial thalamus, are more severely affected in tremor-dominant PD patients than in akinesia/rigidity-dominant PD patients (Paulus & Jellinger, 1991). Jellinger (1999) also reported that loss of dopaminergic cells is more pronounced in the medial portion of the substantia nigra pars compacta (SNc) in tremor-dominant PD, whereas in akinesia/rigidity-dominant PD, greater cell loss is seen in the ventrolateral portion. These clinicopathological findings suggest that tremor could have a different pathophysiology from akinesia/rigidity in PD patients.

3.2 Magnetoencephalography (MEG)

MEG studies in PD patients suggest a critical role of tremor oscillations in the pathophysiology of akinesia and rigidity (Timmermann et al., 2003). Double tremor oscillations in β range are not coherent with simultaneously recorded tremors (Raz et al., 2000; Lemstra et al., 1999; Hurtado et al., 2005). However, a strong coherence at β range is observed in the primary motor cortex, supplementary motor cortex, premotor cortex, diencephalon (possibly thalamus), and contralateral cerebellum (Timmermann et al., 2003). Interestingly, this coupling can be successfully reduced by dopamine replacement therapy (Salenius et al., 2002; Pollok et al., 2009). Simultaneous recordings using MEG and local field potentials in the subthalamic nucleus (STN) reveal that α and β activities are coupled to temporal brain areas and are involved in a functional separation of basal ganglia-cortex loops with different frequency patterns (Hirschmann et al., 2011). Litvak et al. (2011) reported that in PD patients at rest, α-range activities are coupled with temporoparietal-brainstem areas while β-range activities are coupled with the frontal network. Thus, it is likely that β-range oscillations might correlate with the motor loop and with manifestations of akinesia and rigidity.

3.3 Local field potentials (LFPs)

Intra- and postoperative LFP recordings from DBS electrodes provide further evidence that in patients with PD, synchronized tremor frequency oscillations (α or θ range) are coherent with neuronal oscillations in the motor cortex, as are double tremor frequency oscillations at

β range with the globus pallidum internus (GPi) and STN (Levy et al., 2000; 2002). It has been suggested that dopamine depletion could cause neuronal synchronization in basal ganglia circuitry (Liu et al., 2002) and that dopamine therapy could reduce this synchronization (Levy et al., 2002). Gatev et al. (2006) suggested that dopamine activity may play a role in maintaining circuit segregation under normal conditions. STN LFPs in PD patients show synchronized activity with the basal ganglia; these oscillations occur mainly in the β range (15–30 Hz) (Kühn et al., 2004; Hammond et al., 2007). Both STN-DBS and L-dopa administration either ameliorate this β-range oscillation or shift it to a higher (γ range) frequency (Brown et al., 2001; Kühn et al., 2006). The β-range STN stimulation causes further impairment of movement in PD patients (Brown et al., 2001; Fogelson et al., 2005; Chen et al., 2007; Eusebio et al., 2008). These LFP oscillations correlate with akinesia and rigidity but not with tremor (Kühn et al., 2004, 2005, 2006, 2009). In fact, akinesia and rigidity increase when the patients are stimulated at a frequency of 20 Hz (Fogelson et al., 2005; Eusebio et al., 2008). The α-range oscillations in patients with tremor-dominant PD show finely segregated muscle-specific subloops that strongly correlate with the tremor-affected muscles, and tremor suppression can be achieved using STN-DBS in areas with pronounced α oscillations (Reck et al., 2009, 2010). Given that basal ganglia β oscillation correlates with rigidity and akinesia and α oscillation correlates with tremor, these findings further suggest a differential pathophysiology between akinesia-rigidity and tremor.

3.4 Single cell recordings

So-called "kinesthetic" cells receive afferent inputs from muscle spindles and respond to passive joint movements. These cells are located just anterior to the nucleus ventralis caudalis (VC), which receives tactile sensory inputs (Ohye & Narabayashi, 1979; Ohye et al., 1989). Percheron et al. (1996) postulated that the kinesthetic zone is located in the latero-ventral part of the Vim nucleus, a region that sends a majority of its axons to the motor cortex. Vitek et al. (1994) reported that in a monkey model of PD produced using 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), the kinesthetic zone expands anteriorly into regions that contain the active movement-related neurons. Kiss et al. (2003) reported that in patients with tremor, there is an anterior expansion in representation of the movement-related (kinesthetic) neurons without a change in their receptive field sizes. They suggested that tremor activates receptors responsive to deep sensations and, to a lesser degree, superficial sensations; thereby, repetitive tremor activities could result in a gradual increase in the synaptic efficacy of somatosensory inputs to movement-related neurons. Cells that respond to both somatosensory inputs and active movements are referred to as "combined" cells (Lenz et al., 1990, 1994) and have been identified only in patients with movement disorders.

Cells in the VL thalamic nucleus that demonstrate a discharge pattern with burst frequencies similar to that of tremor are called "tremor cells" (Lenz et al., 1988; Ohye et al., 1974). In a monkey model of resting tremor produced by a lesion of the ventral tegmentum, thalamic activity related to tremor frequency is unchanged following the interruption of sensory inputs (Lamarre & Joffroy, 1979; Ohye et al., 1970). This finding has led to the hypothesis that the tremor cells may represent a central pacemaker of tremor genesis, independent of sensory feedback (Lamarre & Joffroy, 1979; Lee & Stein, 1981). Tremor cells are reportedly located in the Vim nucleus and Vo complex (Lenz et al., 1994; Kobayashi et al., 2003; Brodkey JA, 2004). The distribution of tremor cells is important for thalamic

surgery, because tremor has been successfully treated when the radiofrequency lesion was centered within the cluster of tremor cells (Hirai et al., 1979; Nagaseki et al.,1986; Ohye,1979). However, recent studies show that tremor cells are widely distributed in the Vim, Vo, and Vc nuclei, and that they show no apparent differences in proportion within each nucleus (Kobayashi et al., 2003; Brodkey et al., 2004). These findings suggest that the ideal surgical target might not be determined by microelectrode recordings of tremor cells alone (Kobayashi et al., 2003; Katayama et al., 2005). The number of tremor cells in PD patients is much higher than that in patients with other movement disorders, such as essential tremor and multiple sclerosis. This may play a role in the better surgical outcomes seen in PD patients (Brodkey et al., 2004). Based on their experiences, Katayama et al. (2005) postulated that tremor cells might play a predominant role in the lateral portion of the Vim nucleus, which provides the best control of PD-associated tremor, in accordance with previous reports (Atkinson et al., 2002; Hariz & Hirabayashi., 1997).

3.5 Positron emission tomography (PET) and single photon emission computed tomography (SPECT)

PET measurements of local cerebral blood flow (CBF) are used to determine changes in afferent activity onto target synaptic fields or in local neuronal activity, including those of local circuit interneurons, rather than changes in efferent activity. It should be noted that changes in cortical blood flow may not reflect the direct effects of DBS but rather, may reflect sensory feedback from changes in motor activity (Perlmutter & Mink, 2006). The metabolic rate of glucose (CMRglc) measured with (^{18}F)fluoro-2-deoxy-$_D$-glucose PET (FDG-PET) is known as a marker of integrated local synaptic activities and is sensitive to direct neuronal and synaptic damages and to the functional changes in synaptic activity distant from the primary site of pathology (Magistretti et al., 1999).

A recent PET study suggests that the metabolic pattern of tremor-dominant PD is significantly different from that of akinesia/rigidity-dominant PD (Mure et al., 2011). Patients with tremor-dominant PD exhibit better clinical prognoses and slower disease progression with less cognitive decline (Louis et al., 1999; Marras et al., 2002; Rajput et al., 2009). Using FDG-PET, Mure et al. (2011) indicated that these clinical findings correlate with a slow deterioration of the metabolic pattern in patients with tremor-dominant PD. As a significant increase in regional metabolism is found in the rostral cerebellar cortex, dentate nucleus, dorsal pons, putamen, and primary motor cortex, Mure et al. (2011) suggested that both the cerebello-thalamo-cortical pathway and the basal ganglia circuitry are involved in tremor genesis. In patients with PD tremor, high-frequency stimulation of the Vim nucleus reportedly reduces regional metabolism and CBF in the ipsilateral sensorimotor cortex (Parker et al., 1992; Boecker et al., 1997; Wielepp et al., 2001; Mure et al., 2011) and the contralateral dorsal cerebellar nucleus (Parker et al., 1992; Davis et al., 1997; Mure et al., 2011). Interestingly, increases in regional CBF and metabolism are also found in the Vim nucleus ipsilateral to the stimulation site (Rezai et al., 1999; Perlmutter et al., 2002; Haslinger et al., 2003; Fukuda et al., 2004; Mure et al., 2011).

SPECT using Iodine-123 fluoropropyl-carbomethoxy-3 ([^{123}I]FP-CIT SPECT) targets the dopamine transporter and is used to determine ongoing loss of dopaminergic neurons in PD patients (Kaufman & Madras., 1991; Niznik et al., 1991; Seibyl et al., 1998). [^{123}I]FP-CIT SPECT shows significantly higher uptake in the putamen and caudate nucleus in tremor-dominant PD than in akinesia/rigidity-dominant PD (Spiegel et al., 2007; Eggers et al., 2011).

3.6 Functional magnetic resonance imaging (fMRI)

Intrinsic blood oxygen consumption detected by fMRI is correlated with respective low-frequency electrical amplitude fluctuations in classical frequency bands (Logothetis & Wandell, 2004; Laufs et al., 2003; Leopold et al., 2003; He et al., 2008; de Munck et al., 2009). Patients with PD show increased overall activity in networks coupled to the primary motor cortex and cerebellum and reduced functional connections in the supplementary motor area, dorsolateral prefrontal area, and putamen (Wu et al., 2010). Recently, increased functional connections between the STN and cortical motor areas have been found in the resting phase in PD patients (Baudrexel et al., 2011). High-frequency stimulation of the Vim nucleus at an amplitude of 2–4 volts, a frequency of 150 Hz, and a pulse width of 60 μsec reportedly causes metabolic activation of the lateral thalamic wall, GPi, and primary sensorimotor cortex (Rezai et al., 1999).

4. Thalamic deep brain stimulation in Parkinson's disease

The therapeutic mechanism of thalamic DBS remains speculative. With respect to tremor suppression, 4 different hypotheses of Vim-DBS have been proposed. The first proposed mechanism is "conduction block." This hypothesis is supported by the fact that Vim thalamotomy has similar effects to Vim DBS (Benabid et al., 1996). A second possible mechanism involves activation of inhibitory axon terminals that synapse onto and inhibit projection neurons (Wu et al., 2001). A third alternative suggests the superposition of continuous stimuli onto rhythmically oscillating subcortical-cortical loops (Montgomery & Baker, 2000). A final hypothesis is that high-frequency stimulation inhibits neuronal activity near the stimulation site while activating axonal elements that leave the target structure (Vitek, 2002). Recent reports have shown that during high-frequency stimulation, glutamate and adenosine are increased in a calcium-dependent manner, and that these neurotransmitters might be largely derived from astrocytes (Lee et al., 2004; Anderson et al., 2004, 2006; Bekar et al., 2008; Chang et al., 2009; Agnesi et al., 2010; Tawfik et al., 2010). It is hypothesized that this elevated glutamate release excites local interneurons, thereby increasing the production of inhibitory neurotransmitters (e.g., GABA and glycine) and resulting in a decrease in the firing rates of projection neurons (Kang et al., 1998; Fellin & Haydon, 2005; Tian et al., 2005; Fellin et al., 2006; Tawfik VL, 2010). Holsheimer et al. (2000) have suggested that in human brains, the effect of Vim DBS could be mediated through the stimulation of afferent and efferent axons rather than stimulation of cell bodies.

In patients with tremor-dominant PD, tremor suppression can be achieved irrespective of age, disease duration, or baseline disease severity (Benabid et al., 1996; Schuurman et al., 2008). Complete arrest of tremors is usually achieved immediately using continuous stimulation of the Vim nucleus at a high frequency (greater than 100 Hz); these effects are completely reversible (Benabid, 1996).

4.1 Programming challenges in Vim DBS

With stereotactic surgical techniques, the stimulating DBS leads are implanted into the Vim nucleus (Fig. 2). Lesion-like effects of implant are always obtained immediately after the implantation of DBS leads, unless the electrode is misplaced. Initiation of programming is ideally started when the lesion-like effect has almost disappeared. The optimal stimulating parameters are determined using monopolar or bipolar stimulation. For example, first a

constant pulse width of 60 sec and a constant frequency of 130 Hz (or above) is selected. Then the voltage is progressively increased to find the threshold for symptom suppression without adverse effects, using the contact(s) that gives the best effect. As the effect of the stimulation tends to decrease in the weeks or months following surgery and as the threshold for side effects tends to increase, the voltage may have to be further adjusted. Best results are usually obtained at pulse frequencies of 130–185 Hz (no lower than 100 Hz), pulse widths of 60–90 μsec, and amplitudes of 1.5–3.6 volts. Intermittent use of implantable pulse generators is recommended to avoid the development of tolerance (habituation) and to save battery life.
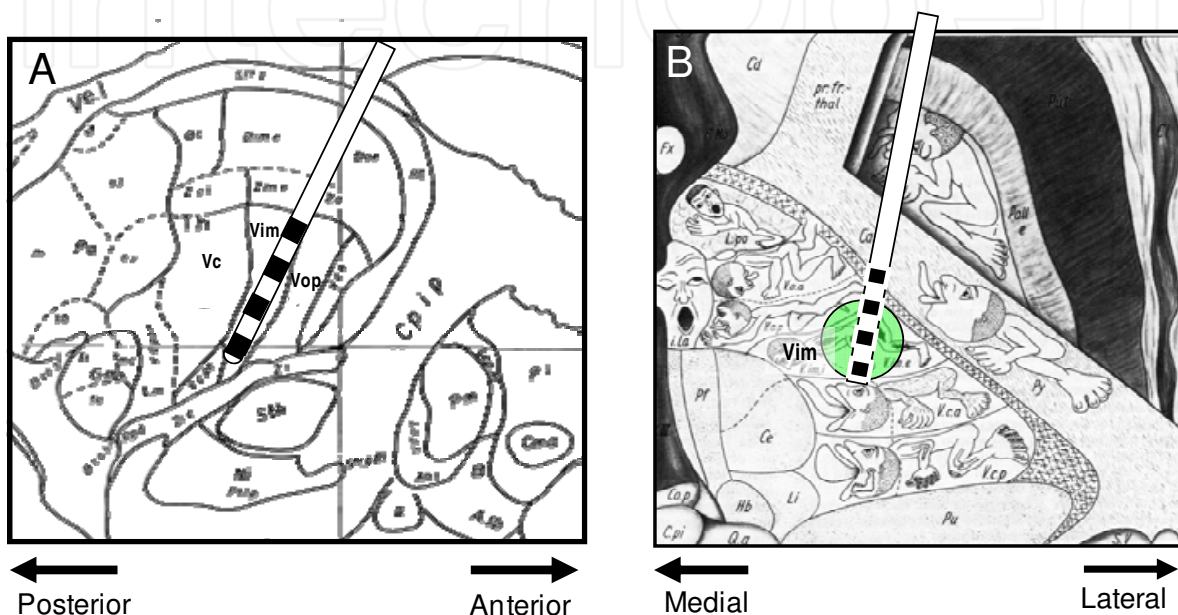

Fig. 2. Schematic drawing of the DBS lead implanted into the Vim nucleus on the the saggital (A) and axial (B) planes of the brain atlas.

4.2 Therapeutic impact of Vim DBS

In early studies with a short-term follow-up (range; 0–40 months), complete or nearly complete tremor resolution was accomplished by Vim DBS in 70–100% of treated patients (Blond et al., 1992; Pollak et al., 1993; Alesch et al., 1995; Benabid et al., 1996; Tasker, 1998; Schuurman et al., 2000; Krauss et al., 2001; Yamamoto et al., 2004). Tremor reduction rate was found to be 71–97% by using the UPDRS Part III motor scale (Hariz et al., 1999; Limousine et al., 1999; Lyons et al., 2001; Kumar et al., 2003; Rehncrona et al., 2003) and 88–93% by using the Tremor Rating Scale (TRS) (Putzke et al., 2003). Based on blind assessments, all the treated patients showed complete or nearly complete relief until at least 2 years after the operation (Schuurman et al., 2000). Assessments with UPDRS Part III revealed tremor reduction rates of 75–83% in the arm and 0–87.9% in the leg (Ondo et al., 1998; Rehncrona et al., 2003). With respect to the long-term efficacy of Vim DBS, Schuurman et al. (2008) reported that 88% of patients showed complete or nearly complete tremor suppression after a mean follow-up period of 5 years, similar to findings of other reports (Kumar et al., 2003; Pahwa et al., 2006; Hariz et al., 2008). Non-tremor parkinsonian symptoms usually remain unchanged at both short- and long-term follow-up points after Vim DBS (Blond et al., 1992; Pollak et al., 1993; Alesch et al., 1995; Benabid et al., 1996; Ondo et al., 1998; Rehncrona et al., 2003; Tarsy et al., 2005; Pahwa et al., 2006; Hariz et al., 2008). However, some reports have shown beneficial

effects of Vim DBS on akinesia, rigidity, and L-dopa-induced dyskinesias (Blond, 1992; Tasker, 1998; Limousin et al., 1999; Putzke et al., 2003; Rehncrona et al., 2003; Pahwa, 2006). These additional benefits of Vim stimulation are thought to be due to spreading of the current to the Vo nucleus area that receives pallidal afferents. Additional stereotactic interventions have been used to treat parkinsonian symptoms that could not respond well to thalamic ablation surgery (Goto et al., 2004) or DBS (Nishio et al., 2009)..

Significant improvements in activities of daily living (ADL) scores have been seen after a short-term follow-up (Blond et al., 1992; Alesch et al., 1995; Koller et al., 1997; Hariz et al., 1999; Limousine et al., 1999; Schuurman et al., 2000; Putzke et al., 2003); however, these scores often return to preoperative baseline or even below during long-term follow-ups (Pahwa et al., 2006; Hariz et al., 2008; Schuurman et al., 2008). Putzke et al. (2003) reported that benefits of Vim-DBS on ADL scores persist for the first 24 months after surgery, but disappear after 36 months. It is necessary to increase dosages of anti-parkinsonism drugs in parallel with disease progression, particularly during long-term follow-ups. In addition, the stimulus amplitude often needs to be increased due to progression of disease and/or the so-called "tolerance" phenomenon, which is also known as "habituation" to electrostimulation of the neuronal network (Benabid et al., 1996; Koller et al., 1997; Hariz et al., 1999). This increase in amplitude is undesirable, as it often causes paresthesia and cerebellar adverse effects (Benabid, 1996; Yamamoto et al., 2004). Recurrence of tremor is seen in ~5% of patients several weeks or years after the surgery (Benabid et al., 1996; Tasker, 1998). Neuropsychological assessments have shown that thalamic DBS results in a significant improvement in verbal memory (Tröster et al., 1998; Hugdahl and Wester, 2000; Woods et al., 2001), conceptualization, and emotional adjustment (Woods et al., 2001), while its left-side stimulation is reported to decrease verbal fluency (Schuurman et al., 2002).

4.3 Adverse events related to Vim DBS

Incidences of stimulation-related complications reported at long-term (greater than 5 years) follow-up include paresthesia (4–38%), dysarthria (3–36%), dystonia/hypertonia (3–16%), gait disturbance (11–16%), balance disturbance (5%), and cognitive dysfunction (2%). Among these adverse effects, non-adjustable and long-lasting complications include dysarthria (10–27%), paresthesia (16%), gait disturbance (7%), dystonia (5%), upper limb ataxia (3–4%), and disequilibrium (3–4%) (Rehncrona et al., 2003; Pawha et al., 2006; Tarsy et al., 2006; Hariz et al., 2008). Pahwa et al. (2006) described occurrences of persistent complications including dysarthria, disequilibrium, and gait disturbance after bilateral stimulation, even when the stimulus parameters were optimized.

The incidence of infection appears to be 0–11% during the early follow-up periods and 0–8% throughout the entire postoperative course (Rehncrona et al., 2003; Tarsy et al., 2006; Hariz et al., 2008; Schuurman et al., 2008). Hardware failures are occasionally found in the stimulator (0–3%), the DBS lead (0–8%), or the cable (0–3%), and skin erosion (0–4%) and hematoma requiring evacuation of the stimulator (0–3%) have also been reported (Rehncrona et al., 2003; Tarsy et al., 2006; Hariz et al., 2008; Schuurman et al., 2008).

5. Conclusions

In conclusion, Vim DBS is an appropriate first-line treatment for medically intractable tremor. Although the effect on ADL outcome decreases gradually after the surgery, long-

term tremor suppression remains stable. STN DBS is currently considered the preferred surgical procedure in patients with tremor-dominant PD, even when disease progression is taken into consideration (Krack et al., 1997). However, STN DBS carries a potential risk of neuropsychiatric problems, particularly in aged patients. We suggest that Vim DBS is useful for patients with tremor-dominant PD, due to slow progression of disease and good response of non-tremor PD symptoms to dopaminergic therapy. We consider patients with intractable upper tremor to be good candidates for Vim DBS.

6. Acknowledgement

7. References

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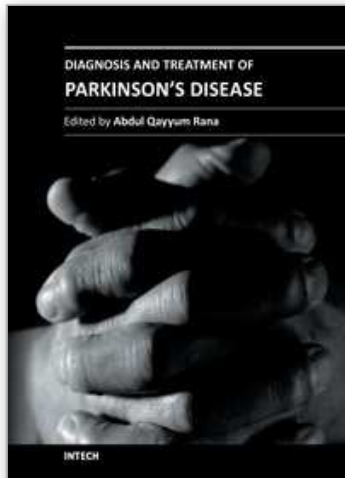
Diagnosis and Treatment of Parkinson's Disease

Edited by Prof. Abdul Qayyum Rana

Parkinson's disease is diagnosed by history and physical examination and there are no laboratory investigations available to aid the diagnosis of Parkinson's disease. Confirmation of diagnosis of Parkinson's disease thus remains a difficulty. This book brings forth an update of most recent developments made in terms of biomarkers and various imaging techniques with potential use for diagnosing Parkinson's disease. A detailed discussion about the differential diagnosis of Parkinson's disease also follows as Parkinson's disease may be difficult to differentiate from other mimicking conditions at times. As Parkinson's disease affects many systems of human body, a multimodality treatment of this condition is necessary to improve the quality of life of patients. This book provides detailed information on the currently available variety of treatments for Parkinson's disease including pharmacotherapy, physical therapy and surgical treatments of Parkinson's disease. Postoperative care of patients of Parkinson's disease has also been discussed in an organized manner in this text. Clinicians dealing with day to day problems caused by Parkinson's disease as well as other healthcare workers can use beneficial treatment outlines provided in this book.

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