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Original Research Article

Analysis of holmes tremor deep brain stimulation of ventro-intermediate thalamic nuclei and posterior subthalamic area

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ABSTRACT

Background: Holmes tremor (HT) is rarely seen in Parkinson's. In our recent investigation, we encountered a Parkinson patient with HT. The subject (patient) was diagnosed through HT-DBS ventro intermediate thalamic nucleus (VIM) plus posterior-sub thalamic-area (PSA) was done.
Objective: the aim was to validate our results with clinical features, etiology, outcomes as of neuroimaging, plus therapy findings in Parkinson's.
Materials and Methods: Patient underwent numerous medications (Carbidopa, Levodopa, and mixed, benzazepines as well as tri-hexy-pheni-dyl). We applied the quantitative-techniques of Fahn-Tolosa-Marin Tremor-Rating-Scale (F.T.M.T.R.S) to measure the degree-of shaking-palsy/tremor. The scoring is a broadly utilized for measuring the tremor. The scale (measuring-tool) included the scoring-scale of the tremor site (portion A), the movement (portion B) plus functional-role (portion C). Subject scoring with F.T.M.T.R was56 plus he cannot handle the any objects, nor he sign nor scribbles nor he sign the signs nor draw the spirals-of-Archimedes. We measured the patients' Holmes tremor using F.T.M.T.R.S at 30, 90-, 180-, 365-, and 730-days following electrical stimulations via minimally invasive deep brain stimulators.
Results: On investigation, there was no improvement in symptoms reduction or restoration, increasing motor functioning restoration. There was no antiquity of consuming by means of neuroleptics and/or shaking palsy(tremor) persuading medicine in advance of or following the brain stem hemorrhage plus there was no genetic-hereditary and/or transmissible family-antiquity of the Parkinson's disease (PD)and/or movement-disorders(MDs).
Conclusion: The outcome demonstrated that the DBS reassured the patient's tremor throughout 730-days (i.e., 24 months – 2 years) follow-up passé or retro.

1. Introduction

A first report case study on mid brain disease was firstly described by the Benedikt in the year 1889 and labelled the tremor as resultant to the mesencephalic infarction, as a 3Hz – 4Hz flexor-point-of-extension oscillations, existing at balance and rest plus aggravated, exacerbated, impaired and intensified and worsened, through the position or posture furthermore intensified by the act and movement (action-movement).[1,2] This HT is termed as rubral, mesencephalic, or thalamic tremor well, yet, these are not applied anymore due to the normal predictable and standard cases were labeled through the lesions situated at some other regions/ or zones, plus 'red-nuclei' investigational-lesions collapse to provoke the tenacious shaking-palsy.[3] Present Holmes tremor is derived as of Consensus Statement of the Movement Disorder Society (CSMDS) over the tremor 1998

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onwards.

The HT is explained as a relaxation (rest) as well as objective (intention) tremor through occasionally random (abnormal improper variable) amplitudes. Yet, postural shaking palsy is furthermore exhibit in several diseased conditions. As it is characteristic, (symptomatic) indicative and suggestive indicative tremor, studies through the medical diagnostic imaging are typically irregular, albeit in specific cases no lesions are cannot be confirmed or exhibited.[1–4] Usually, the tremor develops and occur amid 30 days and 730 days, i.e., 1 and 24 months following the central nervous system (CNS).

Tremor commonly develops between 1 and 24 months after a CNS slight upset. Such prolonged inception/onset possibly will be because of neural/neuronal or neuronic synthetic shaping transforms.[1–3]

Quite it is amused and anticipated that a binary duple-lesion is necessary to creäte the Holmes tremor, involving together through the dopaminergic nigro-striatal-system as well as the cerebello thalamo cortical and/or dentate rubro olivary paths and routes.[4–7] Generally, it is well-known that the pharmacological dealing is futile, even though L-Dopa drug has offered gain within few cases, yet surgical-procedure is optional for the drug-resistant cases and issues.[8]

In this study, we define the sporadic case-of the Holmes tremor secondary to intra cerebral hemorrhage situated at the left (leftward) mid brain to pons Varolii which was efficaciously and also magnificently enhanced through the concurrent instantaneous (yet synchronized in a real-time) DBS of the ventro intermediate thalamic nucleus, or nuclei (VIM) plus posterior subthalamic-area(PSA).[9–12] The greatest frequent and widespread causes of HT in our study was vascular-lesions. The majority and the regular or usual-lesion topography was mes encephalic, thalamic, and/or both. Management through the Levodopa plus thalamic stereo tactic lesional surgical procedure is applicable and most helpful apparently.[13,14] In this study we accomplished the advanced idiopathic Parkinson disease with HT diagnosis. Approval of ethical committee and written informed consent following the Helsinki principle done.

2. Materials and Methods

A 53 year‘s old Parkinson diseased candidate with 120 days antiquity of the tremor distressing and most of the time upsetting the upper-limb of left-hand. A year before he was developed left-limb impassiveness secondary to the hyper tensive brain stem hemorrhage. Then, at that moment point and juncture, the computed axial tomography (CAT), i.e., brain computed tomography (CT) presented the acute hemorrhage within the rightpons neighboring the red-nuclei (nucleus) as depicted in the images (Figure 1 A, and B). Following a fortnight time, the brain stem hemorrhage, 7 Tesla functional magnetic resonance imaging (fMRI) exhibited that the brain stem hemorrhage was positioned within the his arms right-pontine, using the confined brain tissue obliteration (Figure 1 C, and D).

Following the moderate administration conventionally plus physiotherapy, approximately circa ~ 150 days advanced, the diseased can look after himself moderately and also can have his coffee and have food self-sufficiently through his dysfunctional-hand, i.e. left hand. Then, following 180 days, the Homes-tremor progressively seemed within the upper-limb of left-hand, viewing advanced exacerbation and/or magnification. At that point-of-time, the axial T 2 - weighted MR images verified encephalomalacia encephaloma Latic-vicissitudes some sort of fluctuations, cystic deterioration, plus hemo sider in round the graze, i.e., abrasion lesion,(Figure 1 E, and F).

The diseased subject underwent numerous medications which includes Carbidopa, Levodopa, plus carbidopa and levodopa mixed, benzazepines as well as tri-hexy-phenidyl, yet there was no improvement in symptoms reduction or restoration, increasing motor functioning restoration. There was no antiquity of consuming by means of neuro leptics and/or shaking palsy(tremor) persuading medicine in advance of or following the brain stem hemorrhage plus there was no genetic-hereditary and/or transmissible family-antiquity of the Parkinson‘s disease (PD) and/or movement-disorders (MDs). Unlike the subjective unified Parkinson disease rating scale (UPDRS), we applied the quantitative-techniques of Fahn-Tolosa-Marin Tremor-Rating-Scale (F.T.M.T.R.S) to measure the degree-of the shaking-palsy/tremor. This scale, the F.T.M.T.R. scale scoring is a broadly utilized for measuring the tremor and thus is a measuring-tool, which includes the scoring-scale of the tremor site, which is the portion A, the movement, which is the portion B plus the functional-role which is the portion C. His scoring with the F.T.M.T.R. scale was56 plus he cannot handle the any objects, nor he sign nor scribbles, nor he sign the signs nor draw the spirals-of-Archimedes.

As per the observation through the testing of symptoms through the medical imaging plus signs-of-patient medical-antiquity (the history), he was primarily identified as Holmes tremor candidate.

We decided to adopt VIM+PSA double targets. Needle design: Through the planning system, VIM nuclei and PSA area are designed at the same time, and then the electrode puncture path is designed, so that the electrode takes PSA area as the target point and passes through VIM nuclei at the same time.

2.1. Implantation of electrodes through DBS surgical procedure

Through the DBS surgery, the electrode implantation was done unilaterally (one side, i.e., left hemisphere). Anesthesia was given locally by a qualified anesthetist. The

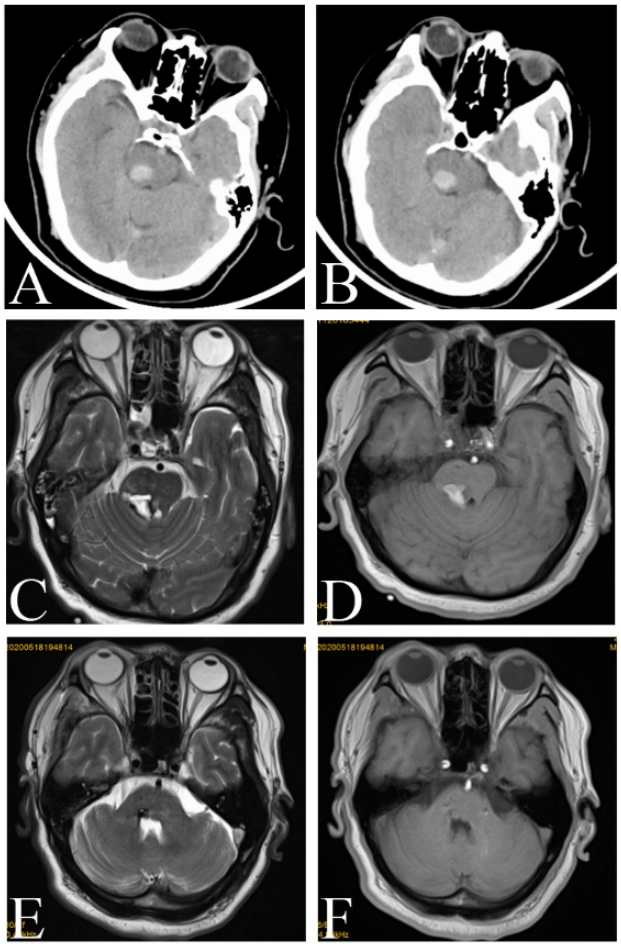

Figure 1: A and **B**: Pre op computed-axial-tomography (CAT) brain imaging displaying critical intra cerebral hemorrhage within the accuratepons neighboring the red-nuclei; **C** and **D**; The magnetic resonance imaging presented the brain stem hemorrhage which was situated within his arms precise-pontine; **E** and **F**; The pre op T-2 as well as T-1 - weighted axial magnetic resonance imaging close-fitting the dynamic-resolution of hemorrhage. The encephaloma Latic variations, cystic-deterioration, as well as hemo sider in round the abrasive laceration (i.e., lesion) were engrossed as well.

CRW frame (stereotactic) plus fusion imaging i.e., CAT and fMRI fused guided directing through the CRW surgical plan. The enduring quadri polar electrodes, model#3387s of Medtronic was inserted.

The single unit single track micro electrode signal acquisition recordings (MERs) were done plus the activity-of-cell was gathered opening as of ±10mm target of the V.I.M. The ventral thalamic margin as well as cells-tremors within the V.I.M. was detected.

Following the configuration and conformity of tip of the electrode that reached sensed the accurate target i.e., of the PSA plus and passing via the V.I.M., the electrode was detached, and the everlasting microelectrode model#3387S of the was embedded and finally intra op macrostimulation test done and this is to confirm the prevention-of-tremor in absenteeism of induced stimulus dyskinesias. While on surgery, i.e., the D B S is ON, symptoms of Parkinson candidate left upper limb tremors were perceptibly reassured exclusive of palpable dyskinesias. Post op CAT imaging was done plus fused with pre op functional magnetic resonance imaging fMRI to prove and validate the point-of-electrode (PoE). Findings demonstrated that the PoE was correct, plus it passes over the two organs, the V I M as well as the P S A instantaneously (Figure 2A,B, and C).

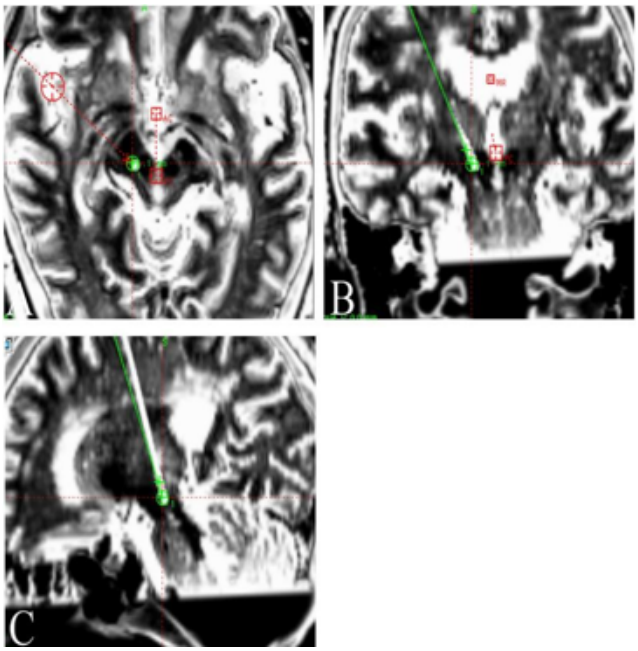

Figure 2: A,B,C: The merged outcomes of pre op fMRI plus post op CAT demonstrate that the PoE of DBS was exactly on those, the then leads passes over the two organs, i.e.,V I M as well as the P S A concurrently.

Moreover, in merger or combining through the surgical Atlas-mapping, we established and inveterate that the distal sensors, microelectrodes that are contacts with the 0 plus 1, were located at the P S A as well as the proximal-microelectrodes, i.e., through the contacts 2 plus 3 at the V I M. The embedded deep brain stimulating electrode was coupled hypodermically, subcutaneously, i.e., intravenously to the implanted pulse generator, i.e., I P Gs, which was rooted within the infra clavicular region in global anesthesia (the anesthesia was given by the qualified anesthetist).

3. Findings

Upon on findings, the diseased subject practiced a noteworthy decrease of shaking-palsy, i.e., the tremor as of the micro lesion upshot. The stimuli were started exactly

following 30 days of DBS surgery. The constraints, i.e., limits/parameters were titrated to stipulate ideal shaking palsy rheostat exclusive of any dyskinesias. The DBS parameters were set as follows: the primary setting of DBS has had the stimulus intensity 1.5volts, amplitudes pulse-width 90 micro-seconds (μ-Sec), plus the frequency at 130Hz through the configuration of the sensing-electrode with zero (0) minus contact, plus, the computer object-oriented C++ Programming language +Ve(positive) with a strong debugger (error remover).

Once stimulus applied over the maximum active connection, the score of FTMTR scoring was fallen to eleven. The diseased subject doesn't show any induced stimulus dyskinesias during the discharge. Yet, because of the candidate steady tolerance to the stimuli, within the resulting 730 days, the sternness of shaking palsy diminished, reduced plus marginally augmented. Throughout the continuation, it was detected that the score of the F.T.M.T.R. scaling rosette only to the 21points, through the stimulus intensity-of 2.4 volts, with a pulse-width-of 90μs followed by the160 Hz frequency.

4. Discussion

In this study, we discussed a case report-of Parkinson subject suffering with Holmes tremor clinically diagnosed through the dual-target stimulation by DBS, eager to edify neuroscientists (neurophysiologists, neurologists, electrophysiologists). The Holmes tremor belonging to the extra pyramidal group diseases, that are typically instigated (produced or triggered) due to variations in pathological of the brainstem, cerebellum plus thalamus, midst which thalamus is the utmost tangled frequently.[2] The pathogenesis of it is not known yet, also it's whispered that the cere bellum red-nuclei thalamus alleyway as well as substantia-nigra (SN) - striatum alleyway are injured.[3]

The investigative measures denote to the shaking palsy-tremor accord framed in the year 1998 through the International Association for Dyskinesia:[4]

1. Inert plus premeditated tremor, frequently supplemented through the postural palsy
2. Typically <4 5Hz frequency

The On-set was late, > 30days to 730 days circa following the main disease which has subsequent features:[5]

1. Regularly it is involving proximal limb-muscles.
2. Usually cannot be reassured through the situation, plus L-Dopa and/or receptor agonist-receptor might be resultant.
3. Main abrasion is situated amid mid brain as well as thalamus.
4. Positron emitted tomography and computed axial tomography PET-CT might demonstrate the reduction of 18 F - Dopa acceptance within the ipsi—lateral putamen as well as the 'caudate—nuclei'. Furthermore, the homes tremor is an appearance of the mid brain plus 'red—nuclei'disorder frequently difficult through the hemi-plegia-limb also oculo motoric-nerve-palsy, plus hyper trophic olivary nuclei deterioration, disintegration, erosion, as well as falling apart—degeneration.[6]

The core medicine of holmes-tremor is principally therapeutic-medication, which includes carbidopa, l-dopa, 'decarboxylation-of-peripheral-dopa', the 'inhibitor-enzyme', benserazide, agonist-dopamine, piribedil, piribedils, anti-epileptic medications, clona-zepam, the central dominant fundamental 'cholinergic-receptor' blockers, phenoxides, and Botox –the Botulinum-toxin-injections, and other, if any.[7]

When it comes to the perfect DBS effectiveness, our experience shows that the detecting the target lesion, choosing the electrode and embedding it accurately at the target-region is significant to the effective surgical-procedure.[8] So far, the sub thalamic nuclei(STN), the globus pallidus internus (GPi) followed by the V I M are the target regions for embedding the electrodes in Parkinson diseased patients which progresses the four classes of motoric, and non-motoric symptoms, like tremor, akinesia (Bradykinesia), postural instability and rigidity, memory, cognitive dementia, cognitive impairment, hallucinations, speech, and axial symptoms such as whole body shaking. Amongst those, the S T N plus GPi mostly progress the quantifiable clinical-symptoms, such as the 'resting-tremor (T), the 'myo-tonia' plus akinesia of Parkinson's diseased subjects.[9]

The V I M is imperceptible over the imaging object, which is mostly situated through the geometrical-coordinate points.[10]

1. On the X-coordinate, usually 12 mm to 14 mm, and 11 mm alongside the wall-of tertiary-ventricle, i.e., the third-ventricle.
2. On the Y-axis, the posterior-commissure (PC) point is 5 mm – 6 mm advancing (forward, $\left(\frac{1}{5}\right)$point last to the (behind) 'anterior-posterior (AC)' – 'posterior-commissure (PC)', i.e., AC – PC link. On the Z-axis, it is 1 mm – 2 mm below the (underneath) the'AC—PC'.

The alignment of the P S A over the imaging:[11]

1. Construct the initial straight line which is horizontal at the parallel which is horizontally epicenter of the extreme, determined and thoroughgoing thickness of red-nuclei. Then lure the next-line over the sub thalamic-nuclei axis as of the leading inside to the last-end (rear-end) utmost out-side of sub-thalamic-nuclei. Then mid-point amongst cross boundary of red-nuclei plus median (medical)-boundary of S T N.

Pragmatic (observed) objective co-ordinates of the PSA-nuclei: [12]

1. On the X-axis, it is 10.8 mm – 13.4 mm as of mid-line. Then, on Y-axis, it is 4.7 mm — 7.9 mm following the medical commissure posterior (M.C.P.). Then, on Z-axis, it is 0.7 mm -5.3 mm underneath the M.C.P.

The V I M has the maximum and clear satisfying outcome over the dominant cardinal motor symptom – the tremor. [13]

Hitherto, it was found clinically that through the passageway – the channel route way-of-time, the restorative - therapeutic-outcome of the V I M – D B S over this cardinal motoric-tremor symptom reduced: [14]

1. Resistant to the induced-stimulus DBS.
2. Progression of PD is not the gentle shaking-tremor.
3. At the same time, parallelly, the V I M has had approximately dyskinesias for instance stability issues as well as other side-effects like instrument, user interruptions or noise through the equipment, etc., usually referred to as 'dysarthria's'.

The functional (anatomical—structural) of P.S.A comprises [15] Caudal Zi designated as c.Zi, pallido–thalamic (i.e., pallid thalamic) white-matter/grey-matter, radiation-of-anterior, designated with 'Raprl'.

The therapeutic-result of the P S A – D B S: [16]

1. The P S A might progress the cardinal tremor-motoric symptoms like stiffness, rigidity/ severity, akinesia-Bradykinesia, the rigid-pace plus irregular position of Parkinson diseased candidates' (usually called Parkinson's), as well as meaningfully decrease signs and indications for instance movement and control fluctuatory—oscillations.

The dyskinesias of P S A – D B S: [17]

1. Dysarthria's like cerebello pontine thalamic fiber link, paresthesia (medial colliculus), balance disorder, ataxia, muscle contraction (suspected internal capsule involvement, abnormal muscle tone), transient or short-term side effects are mostly avoidable by program control.

As per the literature, several researchers work, as of 3 facets, [18] the real tremor-prevention, less dyskinesias: stability and steadiness (usually the balance), other side-effects like dysarthria's as aforementioned, plus enduring efficiency, so, it is absolute to implement the V I M plus P S A dual-targets".

Pointer projection (the construction of the needle): [19]

1. By the scheduling planning—system, the V I M nuclei plus the P S A regions are calculated simultaneously, plus the microelectrode perforation pathway is planned, such that the lead (microelectrode) chooses the P S A zone as a point-of-target plus it travels via the V I M-nuclei concurrently. The outcome of the single alone V I M – D B S only within the Holmes tremor Parkinson subjects are not reasonable or suitable. [20] However, in Holmes Parkinson tremor subjects, higher regions stimuli, or, multiple electrode placing might be mandatory. [21] Within the procedure of dual-target construction, care must be given to avoid-sulcus, ventricles as well as intra cranial "blood-vessels". [22] No need of forcing the dual-targets to traverse parallelly while on surgery, therefore, the P S A nuclei is suggested and chosen as primary-choice. [23] Intra op electro physio logical monitoring as well as intra op brief-testing's are real pathways to fix the target object. [24] Finally, in 730 days duration, the sternness of the cardinal motoric-symptom tremor in this case study reduced as well as marginally improved. [25]

5. Conclusions

We diagnosed through the Holmes' tremor and the therapy was done through deep brain stimulation (DBS) procedure ventro intermediate thalamic nuclei (V.I.M) plus posterior-sub thalamic-area (P.S.A). We measured the patients' Holmes tremor through the Fine Tolosa Marin Tremor Rating Scale (FTMTRS) at 30, 90-, 180-, 365-, and 730-days following electrical stimulations via minimally invasive deep brain stimulators. The PSA – DBS is the operative technique to set the Holmes tremor. In the course of clinico research, neuroscientists (electro neurophysiologists, and/or neurologists and neurosurgeons) might contemplate the P.S.A—D.B.S therapeutic-procedure if at all they happenstance Holmes tremor Parkinson's disease subjects, (i.e., patients). Concluded the two-fold (double — target) targeted minimally invasive operating (i.e., surgical) design, such that there might be added supplementary connection choices (or opportunities or possibilities could be) throughout the post op program control.

6. Source of Funding

None.

7. Conflict of Interest

None.

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