A study of the development of aesthetic analogue scale for deep brain stimulus coding to rejuvenate parkinson`s motor functioning

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Abstract
Subthalamic-nuclei deep brain stimulation (STN-DBS) is a therapeutic surgical technique for advanced idiopathic Parkinson`s. The technique engrosses or rivets implanting the electrode into the brain. Besides booting process for precisely embedding innocuous tiny micro-wires (the microelectrodes) via DBS surgical implantation procedure, efficient coding (i.e., programming) is most significant dynamic and flexible factor for a successful diagnosis and clinical outcome. Whilst, DBS procedure is well developed for regulating the neuro stimulations, its encoding remains cumbersome and source limit (restraint control, energy in battery is a constrained resource). While, kinematic and neuronal bio markers (bio signals) have been investigated as potential feed-back mechanism for adaptive closed loop DBS devices (ACL-DBSD) of late, albeit, there is an emerging need for coding approaches for procedures to adjust the stimulus parameters and electrode technical-specifications and analogous configurations in fact precisely. In this study, an aesthetic analogue scale (AAS) for a real-time adjustment of stimulus parameters is tested visually. The stimulus parameters: stimulus-intensity, stimulus-contact and amplitude pulse-width in Parkinson subjects amid DBS-subthalamic-nuclei were optimized based on the patient's subjective AAS evaluation (score). Murkowski distance (Mk_d) was computed to contrast the personage amalgamation of contact selection and pulse-width (amplitude) to the stimulus parameters that resulted from standard coding derived from quantifiable feature manifestations that are clinical-symptoms. There is no statistical significancy amid AAS scale and standard coding in connection with the precise contact of the electrode pulse-width amplitude employed or in connection with the prognostic and/or diagnostic clinical infection and syndrome sternness. Based on the research results according to the data/ information attained in this study imply that analogue-scale and standard coding techniques lead to parity results interim and instantly. Results also indicate that the examining the Parkinson`s subjective rating as an added or supplementary and legitimate pointer signal for fine-tuning of the personalized stimulus regulation.

Keywords: Adaptive Closed Loop (ACL), Aesthetic Analogue Scale (AAS), Deep Brain Stimulation (DBS), Microelectrode, Minkowski Distance (MD), Parkinson's Disease (PD), Subthalamic Nucleus (STN).

Introduction
A number of advances have been taken place in the field of neuromodulation especially for neurodegenerative advanced idiopathic Parkinson`s disease (PD) which includes investigating new structural targets, humanizing—pioneering and frontier-technology. At present, subthalamic-nuclei (STN) are the best and key-target for PD-surgery. For this malady, deep brain stimulation (DBS) is a better suited therapy (at the moment) for cardinal motor-symptoms reduction, mainly tremors and motor fluctuations, and restoring and also increasing the motor functioning.

DBS is a stereotactic functional neurosurgical treatment (procedure) that stimulates the brain with electrical signals, is applied to treat PD and an ever-increasing list of neurological disorders. Despite growing numbers of applications, DBS is a relative technological standstill due to several factors: Limited choice of waveforms, some degree of choice of stimulus waveforms, ability to stimulate on a sole position with limited use of battery. The only acceptable key in input is a periodic or sporadic train of quadrangle pulses applied in an extremely tiny region of the brain (a few millimeters). Even though some degree of customization and custom –built program is allowable (e.g., change of pulse width, frequency, amplitude, etc), the resultant signals—waveforms hog-tied to generate—produce a ample selection of controlled responses from the targeted neural system, restraining the patient's behaviors. It is likely that the curative-impact of such steady periodic stimulation stems from restoring the pathological rhythmic basal ganglia (BG) output seen in PD with stimulant—tonic, high frequency (HF) firing. This augmented movement stops neurons from modulating action in their adjoining or neighboring structures producing an "information-lesion" within the vicinity. HF stimulation provides medical benefits (PD motoric-symptoms reversal) when the targeted region is immensely pathological, yet comes amid major charges: prolonged physical programming of the signal, veto adjustment to patient's needs, frequent surgical battery proxy, and prevalent sway to near cognitive loops with probable adverse face effects.

Since the pioneering work of Benabid et al.[1] deep brain stimulation (DBS) has become a standard treatment for advanced stages of Parkinson's disease (PD), for medically intractable essential tremor (ET), and for complicated forms of dystonia. Apart from the careful selection of suitable patients and the correct surgical device implantation, successful post operative (post op) coding of DBS devices is regarded as to be the most relevant factor for the individual patient outcome.[2-4] Once a patient has been implanted with DBS leads, adjusting stimulation parameters is the only way to optimize the clinical effect and it becomes even more important if DBS electrodes are located outside the center of the intended target structure. DBS parameter adjustment has been shown to ameliorate patient outcomes and to prevent unnecessary lead revisions.[5] In addition, a sometimes

significant advancement with re-programming demonstrates that the correct adjustment of stimulation parameters is a major factor for successful treatment and patient satisfaction.[6] Despite customized strategies for adjusting neuro stimuli,[7,8] the encoding of DBS needed time and special possessions. novel leads with two levels of tri partite microelectrodes (i.e., sub-segmented microelectrodes) shall improve the therapeutic window but increase the number of latent combinations of coding(encoding) parameters.[9] So, there is a need for novel strategies on how to adjust stimulus parameters and micro lead specifications technically and technical configurations in a rapid, precise, and effective way. At present, patient-subject and disease-specific-bio-markers are being actively observed, which can be incorporated into adaptive closed-loop stimulus systems, responding rapidly to real-time patient needs, and avoiding the need for manual programming,[10,11] However, the most suitable biomarker (the bio signal) remains to be determined and likely differs between different disease states and individual patients. Here, we tested the usefulness of the patient's subjective rating as a feedback signal for DBS adjustment. We compared the specific contact and stimulation amplitude resulting from the patient's subjective rating on an AAS with a clinical standard and found no significant difference between the two programming approaches. Our results thus suggest that DBS patients are well able to adjust their IPG by themselves and will support the investigation of the patient's subjective rating as a feed back mechanism signal for DBS programming.

Materials and Methods

Seventeen subjects with idiopathic Parkinson's disease (PD were recruited in this study. All the subjects underwent STN-DBS surgery and had the DBS for a year and were on stable DBS coding for 90 days prior to the study visits. They were inducted through custom regular visits at our tertiary care hospital derived from their concern for chipping in the study and on satisfying the focal insertion criteria, i.e., implanting the pulse generators through diagnostics in to the STN zone with the DBS diagnosis/ or prognosis, i.e., they were inducted as per the UPDRS-stage-III+ scale and UK Parkinson's disease Society Brain Bank Clinical Diagnostic criterion [12].

Visiting the clinic and decoding DBS

Consequently in a shipshape to ordeal the discriminating quantifiable medical-effects of coding through AAS, the subjects were first resoluted the UPDRS-stage-III+, i.e., "medication on and DBS on (med on and DBS on)" prior to the study-visit (Fig. 1).

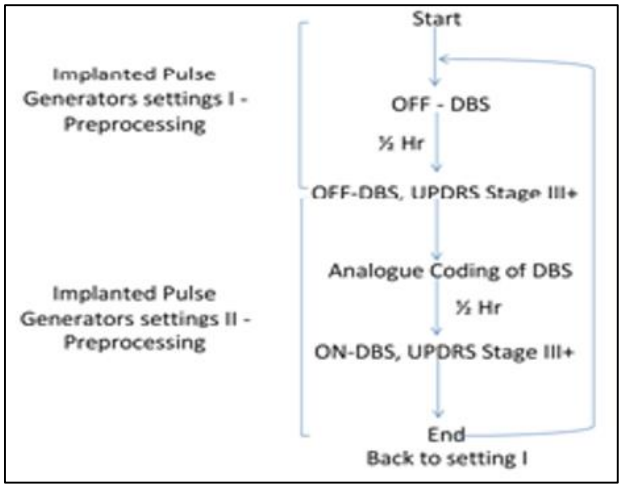

Fig 1 Regulating/ fine-tuning of the pulse generators (implanted) settings through the study-visit.

Flowchart – Procedural Algorithmic steps:

Step#1: Every subject chipped in a single-visit during the study and UPDRS-stage-III+ scale was attained by the DBS ON.

Step#2: The DBS implanted pulse generators were switched off and the study subjects were requested to take rest for a half hour$\frac{1}{2}$, Hr follow by another UPDRS-stage-III+ (OFF-DBS)

Thereafter, the study participants were subjected to VAS-based IPG programming.

Step#3: Following, half hour$\frac{1}{2}$, Hr, a final UPDRS-stage-III+ scale was attained in all subjects through AAS derived DBS coding activated (ON-DBS).

Step#4: The End. Here all the accomplices (participants) were switched back to the IPGs settings

While on medication ('med on'), every subject was checked in pharmaco logically, i.e., exclusive of pausing any medicine aforementioned to the study visit. The precise medicine is specified in every individual subject's medicine (Table 1). Subsequently, the stimulus parameters were texted, the stimuli was switched off on the clinically main side, (i.e., the left hemisphere brain electrode for the right hemisphere brain side). The subjects were requested to seat for a half hour$\frac{1}{2}$Hr@rest prior to the UPDRS-stage-III+ scale, on medication and off DBS\ was once more précised, i.e., calculated. Consequently, all the subjects undergo for an AAS coding for their DBS on the lateral which was toggled off (switched off) prior to. Hence, the subjects were offered by poles apart (dissimilar) pulse-widths and amplitudes from 0 mille-Amperes – 3 mille-Amperes, and 5 mille-Amperes at every (0–3, 5mA) and at each and every entity contact disjointedly. Dissimilar settings both stimulus intensities and pulse-width-amplitudes were showed arbitrarily and also indiscriminately to evade to shun the taming and breathing in. Subsequently every subject with fine-tuning, i.e., setting, the patient was instructed to pace the inclusive quality-of-DBS outcome on a scale 0-9. Hence, all subjects were

requested to pace quality-of existing-settings on the scale 0-9, where, 0 meant for is execrable (repulsive) and 9 is meant for great exclusive of any more elucidation. The values in the middle of were précised any more or explained to subject (because, the evaluation was exclusively prepared derived from the subjective insight and opinion of the subject in a prearranged stimulus-setting or adjustment.

The individual ranking (score) was evaluated following the subsequent. All the subjects were canopy to individual (particular and relevant) stimuli-setting prior to and also at some point in regulating the pulse-generators which were implanted. Opting for and deciding a precise setting analogously taken fourteen seconds duration circa. Following every AAS-setting, a flush-out time circa one minute was upholded proceeding to the arrangement of the subsequent analogue-settings adjustments. The complete setting or adjustment of the analogue scoring procedure taken fourty-two minutes duration per lead (microelectrode) per subject.

Estimation of Murkowski distance

The Minkowski distance or Minkowski (Hermann) cadent is a cadent in a normed vector space which can be considered as a generalization of both the Euclidean distance and the Manhattan distance. Minkowski cadent is a cadent/ parallel dimension amid 2-points in the normed vector space (N dimensional real space) and is a generalization of the Euclidean distance and the Manhattan distance. The Minkowski distance of order p (where p is an integer) between two points is defined as:

$X = (x_1, x_2, x_3, \ldots, x_n)$ and

$Y = (y_1, y_2, y_3, \ldots, y_n) \in R^n$

$D(X, Y) = [\sum_{i=1}^{n} |X_i - Y_i|^p]^{1/p}$

For p >=, the Minkowski distance is a cadent as a result of the Minkowski inequality. When p<=1, the distance amid [1,1] and [0,0] is $2^{1/p}$, but the point [0,1] is at a distance 1 from both of these points. Since this violates the triangle inequality, for p<=1 it is an uncadent. However, a cadent can be obtained for these values by simply removing the exponent of p. The resulting cadent is also an *F-norm*. The goal is to compute the Minkowski distance of order p (which is an integer) amid two variables i.e., between two points. The case where p = 1 is equivalent to the Manhattan distance and the case where p = 2 is equivalent to the Euclidean distance. The Minkowski distance between two variables *X* and *Y* is defined as

$$\left[\sum_{i=1}^{n} |X_i - Y_i|^p\right]^{1/p}$$

In the case of p = 1, which is equivalent to the Manhattan distance and the case of when p = 2 which is said to be equivalent to the Euclidean distance. Even if p is a real value, it can be set to between the values 1 and 2. If p<1, the above principle will not define the legitimatic expanse cadent in view of the fact that the triangles in equality are unsatisfied. The following command is used while computing (coding) the *p*.

Let p = <value> [prior to entering Mirkowski distance command].

If *p* is not a precise default value, then, *p*<= 1 is used.

Computation: The distance was computed as a gauge of connection (parallel) to contrast the stimulus setting and adjustment prior to AAS coding. The anterior posterior lateral and medial points were considered as a target points target electrodes in order to contact and the stimulus pulse-width (amplitude) in every subject and then the Minkowski distance was generated by employing the R program starts 3.6.1 from R Studio (https://www.R-project.org, http://www.rstudio.com).The stimulus-amplitude (measured typically in milliAmperes) and the number of leads – the microwires (microelectrodes) were accustomed for every subject prior to by following the above principle. The greatest stimulus intensity (amplitude) and pulse-width by means of experimental and quantifiable clinically-relevant was distincted as 6.8 mille Amperes. The subjects were selected in this study group due to the highest better stimulus intensity in this study group of subjects selected. The greatest Mirkowski value was set to fifty six, i.e., four dissimilar ring levels × fourteen discrete stimulus pulse-width-amplitude steps.

Results and Discussion

Seventeen subjects (Table 1, n=17), i.e., Parkinson`s were recruited in this study with their mean age at the onset of 61.4±6,2years, duration of the disease was 15.76±2.86years by means of a standard stimulus period of 3.29±2.73yers. Medtronic microelectrodes were put into the subjects. To contrast the unique settings of DBS sequentially the evaluation of AAS results (scores) were acquired for every electrode contact – stimulus intensity and pulse-width voltage-amplitudes (Fig 1) which was effected in seven discrete analogue values visibly: o, 5 – 1 - 1, 5 – 2 - 2, 5 – 3 - 3, 5 milliamps for every contacts checked (Fig. 1 a, and 1 b) that were measured and also recorded discretely. To avoid taming, every PD subject was showed in sporadic amalgamations of stimulus-intensity, contacts and pulse-width voltage-amplitudes sequentially. While contrasting the chosen current-voltage from a customized computer program (medical software), i.e., setting#1, by the current-voltage from AAS-based coding, i.e., setting#2, there was significant variation and so middling PD subjects choose alike stimulus pulse-widths and voltage-amplitudes as the neuroscientists would (Fig 2 a). Similarly, there was no significant difference found amongst the ring-level-height (RLH): one to four amid the two dissimilar settings and also adjustments, and hence, signifying that the subjects also choose parallel levels of microelectrodes during the patient's ratings subjectively (manually, Fig 2 b). Nonetheless these calculations show merely normal differentiations and so may not be appropriate to demonstrate or to exemplify the in general resemblance

among two dissimilar pulse-generators settings. To create a complex and compound-value that integrates lead (microelectrode) level and stimulus intensity and pulse-width voltage-amplitudes, we computed Mirkowski distances for the chosen stimulus-contacts in setting number one (set#1) and in setting number two (set#2) Fig 2 c, correspondingly.

While opting for Parkinson`s, the subjects age, epoch, gender and vertebra (both left and right sides) are précised for every subject alongside the moment in time in view of the fact that the disease-onset, the time-duration because of the embedding the deep brain stimulus devise and the device producer. Additionally, the encoding facts and particulars like stimulus intensity which gives the particular and electrode precise-contact with the target neuron, pulse-width amplitudes followed by the frequency prior to the analog visual encoding technique is précised. The nature of stimuli is precise that demonstrating any ring-mode 'r' or else employing the sub fragments on a set ring-level 'f'. The level of the ring denotes the lead (the microelectrode) pinnacle on a four-level lead, i.e., 1, 2, 3, or 4. In concurrence by our preceding findings, we found a very low Murkowski-distance for two settings in 9 PD-subjects having preferred the very identical electrode level like height, of which six subjects have preferred the equal contact on fragmented leads. Hence, results of this study and combined results imply that analog visual coding leads to analogous findings in connection with the stimulus-amplitude and contact-of-electrode as contrasted to our diagnosis and encoding customarily.

To seek supplementary quantifiable experimental deliver in retort to AAS encoding; the contrasted the UPDRS-stage-III+ scale prior to and following the analog coding (Fig. 3) and results showed that there is no significant difference statistically (Fig 3 a.). Because we were addressing interim and instant findings and because the motoric-tremor-feature in Parkinson`s and it is also a well recognized motor-feature and responds to very well to the deep brain stimulations and so we also differentiated the findings of the tremor evaluating objects of the UPDRS-stage-III+ scale. Also, on comparing with the analog and conventional i.e., subjective UPDS scaling, there was no significant differentiation between these two (Fig 3 b). Combining the results suggesting that analog encoding is likely to result in parallel interim and instant prognostic results as contrasted with usual traditional loom directed by the diagnostic and/or prognostic features.

The deep brain stimulation encoding (coding) has become complicated now with the number of electrodes in core and also because of likely and probable and potential combinations of encoding parameters (stimulus intensity, amplitude pulse-width, and frequency) and augment exponentially.[12]

Rather than the frequent function of quantifiable experimental tests through coding, the Parkinson`s diseased patient's subjective raring personally and possibly as suitable as feed back signal mechanism, as a clinical/ and/or prognostic-test, however simultaneously perhaps lesser period and overriding the source, i.e., resource, and such approach might let for repetitive settings of stimulus parameters by the PD subject in the absence of regular visits to the DBS clinicians centers. This hypothesis has insinuation connotations for the post op care of PD subjects, specifically for individuals who might not be proficient to frequently focus follow-up visits, although has not at all been addressed scientifically hitherto. Hence, in this study, we studied the importance of a analog visual encoding in Parkinson`s. Results showed, a high degree of correlation in the midst of the stimulus adjustments and settings ensuing as of our clinician-encoded customary loom and the adjustments-settings inferred as of analog visual based encoding. Compare

Hence records advices that in Parkinson subjects, the patients opt for a set (i.e., for setting) on their own which is considerably not distinctive or singular as of the situation the skilled clinician had preferred for them. Results of this study concur with recent studies which holds which carries well the power of strength of self estimation in programming with stimulus deep brain.[13] In the future prospective, the experimental investigations are must to evaluate the neuro-clinicians efficacy of the 2 approaches in *de novo* subjects above an unmitigated epoch of instance or moment.

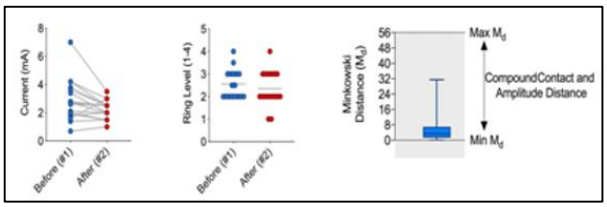

Fig. 2: The analog based visual scale for DBS encoding guides to parity contact and stimulus-amplitudes pulse-width options as regular coding of prognostics. a. voltage selected at 1 which is preprocessing of analog based visual scale, 2 mean-average±s. e. m:2.846±0.3546 versus2.243±0.1546;pearson`s correlation-P>0.05. b. stature of ring-levels:1,2,3,4 on the microelectrode in setting number (pre of analog based visual-scale), 2 is analog based visual scale-mean-average±s.e.m:2.846±0.3546versus2.243±0.1546 (statistically significant (p>0.05). c. Barchart giving the mean-average±s.e.m. The Murkowski-distance (M_d) in view of contact and stimulus-amplitude pulse-widths amid set numbers 1 and 2, mean-average: M_d±s.e.m:5.58 ±7.58). The t-test was conducted for contrast (in Fig. 2 a, and b).

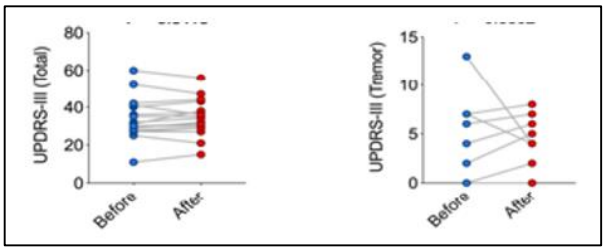

Fig. 3: Analog-based visual encoding tends to interim findings as contrasted to regular encoding of DBS. Fig`s a, and b: depicting the sum of UPDRS-stage-III scale-value (a) and the motoric-tremor symptom discerning UPDRS-stage-III scale-value (b) in all personage subject by setting the

number 1/or setting the number 2: mean-average:±s.e.m:33.97±2.689 versus34.40±2.359, and($p > 0.05$). The t-test was conducted for contrast (in Fig. 2 a, and b) there was a tendency in the direction of a slight stimulus-amplitude ad pulse-width by AAS-based DBS coding.

Also to compute the stimulus-amplitudes pulse-width, levels of the ring too, the Md was selected to compute as a complex gauge to contrast dissimilar stimulus-settings. A stride-size of 0.5 mille-Amperes was preferred and determined as a conciliation among the precision and likelihood, which is compulsory period to recur in the order of sequential analog based enquiries visually). In parallel to the personage-values, and M_d-values are squat linking the two settings. Conspicuously and remarkably, 1 subject had an analog based visual scale (pre) with a voltage of 7 mille Amperes and the Md-value in this subject was upper than in the respite of the group (and our selected voltage levels were 0 mille-Amperes to 3 mille-Amperes, and 5 mille-Amperes). In general, M_d-values emerge to elect a consistent and dependable and functional and valuable gauge to contrast dissimilar pulse-generators adjustments and settings and will sustain the contrast of discrete coding approaches together with potential experimental investigational studies on adaptive closed loop deep brain stimulators. Even if the general stimulus voltage was not considerably dissimilar among the setting-adjustments1 and also 2 (Fig. 2a), there was a tendency in the direction of a minor stimulus-amplitude pulse-widths with analog based visual coding of DBS. Hence, analog based visual encoding might be linked by a condensed stimulus-voltage and hence can aid to tame the drain and exhaustion of the battery but the findings are required to confirm from review studies that observe the analog based visual adjustments and settings above the higher duration and in a improved cohorts of subjects which allows for further vigorous analysis statistically for statistical significancy.

Studies[14-19] have reported that the capability of Parkinson`s is to evaluate their existing condition of movement at present linger a issue of an argument recommended that Parkinson`s able to give precise information on their own of their order of disability and melancholy during cognitive dementia and cognitive impairment, depression, etc.

Because non motoric feature manifestations' such as cognitive impairment dementia and depression and also axial symptoms like slurred speech, and insomnia and hallucinations are not noticed by clinicians and hence patients themselves disclosing[20] in their self reports during their visits to the DBS clinics. Studies.[21-28] also reported alongside the adequate capability of Parkinson`s to precisely rate their deficits redolent of anosognosia in Parkinson`s and movement disorder subjects. Some alertness on their own might associate by axial features[18] and also on the duration of the disease but it is very minimal.

So, researchers have to study the long-term safety and security of analog-based encoding approaches, in scrupulous in connection with neuropsychiatric manifestations for instance melancholy, nervousness, etc. The viability and the safety of DBS analog based encoding approaches for the subject's long term results can be observed by investigating in the clinical experiments in the near future. At our centre, the subjects enrolled. Some of our patients have acquainted through the specific effects such as dysarthrias and also side effects like dyskinesias of deep brain stimulation electrodes and perchance mystifying the strength of our strategy. Potential clinical-trials must evaluate the dissimilar encoding approaches in inexperienced PD subjects to define the impending patient`s subjective score as a suitable legal and safe feed-back-mechanistic signal for deep brain stimuli regulations and amendments.

Conclusion

This study showed better results using the AAS comparing with the subjective rating. However, Prospect studies may address the achievability and practicability and also safety and efficacy of AAS encoding procedures for the Parkinson subjects enduring results for better clinical outcome.

Conflicts of Interest

All contributing authors declare no conflicts of interest.

Source of Funding

None.

References

1. Benabid AL, Pollak P, Gervason C, Hoffmann D, Gao DM, Hommel M et al, Long term suppression of tremor by chronic stimulation of the ventral intermediate thalamic nucleus. *Lancet.* 1991;337:403-6.
2. J. Volkmann, E. Moro, R. Pahwa, Basic algorithms for the encoding of deep brain stimulation in Parkinson's disease. *Mov Disord* 2006;13(21):S284-9.
3. B L Walter, J L Vitek, DBS Surgical treatment for Parkinson's disease. *Lancet Neurol.* 2004;3:719-28.
4. Hans S, Electrical stimulation inhibits cytosine arabinoside-induce neuronal death by preventing apoptosis in dorsal root ganglion neurons. Neuroreport, 2016.
5. VR Raju. Latent Variate Factorial Principal Component Analysis of Microelectrode Recording of Subthalamic Nuclei Neural Signals with Deep Brain Stimulator in Parkinson Diseaseet.al. Springer Briefs in Forensic and Medical Bioinformatics, Soft Computing and Medical Bioinformatics, https://doi.org/10.1007/978-981-13-0059-2_9, Chapter 9, pages: 73-83, 2018.
6. VR Raju, Principal component latent variate factorial analysis of MER signals of STN-DBS in Parkinson`s disease (Electrode Implantation). *Springer Nat*, 2018;68(3):
7. V. Rama Raju, et.al., "The Role of Microelectrode Recording (MER) in STN DBS Electrode Implantation", IFMBE Proceedings, Springer, Vol. 51, World Congress on Medical Physics and Biomedical Engineering, June 7-12, 2015, Toronto, Canada, Pp: 1204-1208, www.wc2015.org
8. Jankovic J, "Parkinson's disease: clinical features and diagnosis". *J Neurol Neurosurg Psychiatry*. 2008;79:368-76.
9. Fahn. S, Elton. RL, The Unified Parkinsons Disease Rating Scale. Recent developments in Parkinsons disease. Florham Park, N.J: Macmillan Healthcare Information; 1987:153-63.
10. Antoniades CA, Barker RA. The search for biomarkers in Parkinsons disease: a critical review. *Expert Rev*. 2008;8(12):1841-52.

11. Morgan JC, Mehta SH, Sethi KD. Biomarkers in Parkinsons disease. *Curr Neurol Neurosci Rep*. 2010;10:423-30.
12. Evelyn Strauss, Lasker Foundation. Lasker~DeBakey Clinical Medical Research Award to Alim Louis Benabid and Mahlon DeLong. Pp: 1-4, 2014.
13. Amirnovin R, Williams ZM, Cosgrove GR, Eskandar EN. Experience with microelectrode guided subthalamic nucleus deep brain stimulation. *Neurosurg*. 2006;58(1Suppl):ONS96-102..
14. Kyriaki Kostoglou, Classification and Prediction of Clinical Improvement in Deep Brain Stimulation from Intraoperative Microelectrode Recording, *IEEE Trans. BME*, 2017;64(5):1123-30.
15. Sang Jin Kim, Kavirakja Udupa, Zhen Ni, Elena Moro, Carolyn Gunraj,et.al, Effects of Subthalamic nucleus stimulation on motor cortex plasticity in Parkinson disease, Neurology, Vol. 85, Pp: 425–432, 2015
16. Bour LJ, Contarino MF, Foncke EM, de Bie RM, Long term experience with intraoperative microrecording during DBS neurosurgery in STN and Gpi . *Acta Neurochir (Wien)*, 2010;152(12):2069-77.
17. Zuan H, Neural Signal processing of microelectrode recordings for deep brain stimulation, Chalmers University of Technology, 2009.
18. Benabid A. L, "Deep brain stimulation for Parkinson's disease," *Curr. Opin. Neurobiol* 2003;13(6):696-06.
19. Benabid A. L, "Acute and long-term effects of subthalamic nucleus stimulation in Parkinson's disease," *Stereotact. Funct. Neurosurg.*, 1994;62:1–4.
20. Moran A, "Subthalamic nucleus functional organization revealed by Parkinsonian neuronal oscillations and synchrony," *Brain* 2008;131(12):3395-409.
21. Defer GL, "Core assessment program for surgical intervention therapies in Parkinson's disease," *Mov. Disord.* 1999;14(4):572-84.
22. Andrade-Souza YM, Schwalb JM, Hamani C, Eltahawy H, Hoque T, Saint-Cyr J et al. Comparison of three methods of targeting the subthalamic nucleus for chronic stimulation in Parkinson's disease. *Neurosurg* 2008;62(2):875-83.
23. Larry Squire, Darwin Berg, Floyd E. Bloom, Sascha du Lac, Anirvan Ghosh Nicholas C. Spitzer, Fundamental Neuroscience, 4th Ed. *AP* Academic Press, 2012.
24. McClelland S 3rd.A cost analysis of intraoperative microelectrode recording during subthalamic stimulation for Parkinson's disease. *Mov Disord.* 2011.
25. William H Press, Saul A. Teukolsky, William T. Vetterling, and Brian P. Flannery, Numerical Recipes in C++, Cambridge University Press, 2002.
26. Andrzej Dobrowolski, Kazimierz Tomczykiewicz, and Piotr Komur, Spectral Analysis of Motor Unit Action Potentials, *IEEE Trans. Biomed. Eng*, 2008;54(12):2300-2.
27. Santaniello S, Therapeutic mechanisms of high-frequency stimulation in Parkinson`s disease and neural restoration via loop-based reinforcement. *Proce of the Natl Acad Sci* 2015;1-10.
28. Sridevi V. Sarma, et.al, Using point process models to compare neural spiking activity in the subthalamic nucleus of Parkinson`s patients and a healthy primate, IEEE Trans Biomed Eng. 2001;57(6):1297-305.

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