

Research Article

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Subthalamic Nucleus Stimulation is Efficient over the Time in Parkinson's Disease: A Clinical Evaluation

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(+)In memory of Bernard Teston who made a great contribution in the achievement of this work. Rest in peace.

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Abstract

Context: The management of Parkinson's disease poses a real problem for the clinician. Stimulation of the subthalamic nucleus is a certain therapeutic hope, even if it does not stop the evolutionary genius of the disease.

Objective: To evaluate the evolution over time of the effect of stimulation of the subthalamic nucleus on clinical parameters of Parkinson's disease.

Patients and Method: The UPDRS scores of 51 patients followed in the context of a neurology consultation were evaluated in ON/OFF STIM conditions. Beyond the overall UPDRS score, sub-scores relating to akineto-rigid signs and axial signs were also evaluated in the context of an experimental study. The statistical analysis used a classical linear model. A threshold of statistical significance was retained for $p < 0.05$.

Results: It appeared that, for the UPDRS global score, there is a significant and persistent ON vs OFF difference in the time interval studied. This difference ON vs OFF was also found significantly and persistently for the subscores relating to the axial signs and the akineto-rigid signs.

Conclusion: Our results show that the effect of stimulation of the subthalamic nucleus on the global UPDRS score and the sub-scores relating to akineto-rigid and axial signs is real and persistent during the time interval studied.

Keywords: Parkinson's disease; Stimulation of the subthalamic nucleus; UPDRS score; Time course; Clinical evaluation

Introduction

Parkinson's disease poses a real problem of management for the clinician insofar as there is no curative treatment. Indeed, the only treatments currently available are purely symptomatic and dominated by L-dopa. However, its effect dissipates over time after a more or less long phase of effectiveness called "therapeutic

honeymoon" [1]. Stimulation of the subthalamic nucleus therefore represents a credible therapeutic alternative because its efficacy on the clinical signs of Parkinson's disease has been proven [2]. Our objective was therefore to evaluate the effect over time of this technique on the motor clinical signs of Parkinson's disease.

Patients and Methods

Patients

Fifty-one patients, followed as part of a neurology consultation and wearing a subthalamic nucleus neurostimulation device, were evaluated in ON STIM (stimulation on) and OFF STIM (stimulation off) conditions at different postoperative time intervals. All patients had previously signed an informed consent.

Methods

The evaluation consisted of establishing the UPDRS motor score for each patient, which corresponds to the third part of this scale for evaluating Parkinson's disease [3]. Alongside the global motor score of the UPDRS, sub-scores relating respectively to the akineto-rigid signs and to the axial signs were also individualized. The sub-score relating to the akineto-rigid signs that we called U_AKIR in this work corresponded in fact to the sum of items 19, 22, 23, 24, 25, 26 and 31. As for the sub-score relating to the axial signs and called here U_AXIAL, it corresponded to the sum of items 18, 27, 28, 29 and 30. The postoperative time interval studied extended up to 100 months and was divided into five sub-intervals (0 to 20

months, 21 to 40 months, 41 to 60 months, 61 to 80 months and 81 to 100 months). For each interval, the average of the patient scores was calculated in ON and OFF STIM conditions.

The statistical analysis used a classical linear model. The significance threshold was retained for $p < 0.05$. In addition, a time threshold at 10 months has been introduced, making it possible to compare the parameters before and after this threshold.

Results

Patients

The patients had a mean age of 61 years (SD= 6.86) with a mean duration of disease progression of approximately 13 years (SD= 4.84).

UPDRS Global Motor Score (U_GLOBAL)

Concerning U_GLOBAL, a significant ($p < 0.001$) and persistent difference ON STIM vs OFF STIM was noted in the considered time interval of the postoperative delay. In addition there is a decreasing trend of U_GLOBAL values in OFF and ON conditions with a significant slope ($p < 0.01$) (Figure 1).

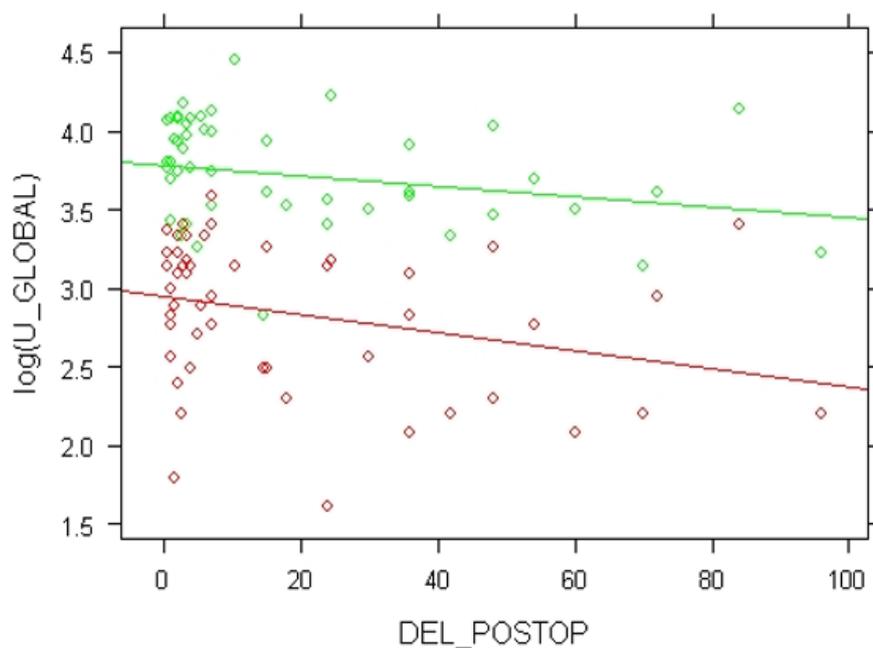


Figure 1: Temporal evolution of U_GLOBAL during the postoperative period (in green the patients in OFF STIM and, in red, the patients in ON STIM). DEL_POSTOP means postoperative period.

Still concerning U_GLOBAL, there was a clear statistically significant difference in level between the scores before and after 10 months: the scores were better after 10 months ($p < 0.01$) (Figure 2).

The Subscore Relating to Akineto-Rigid Signs (U_AKIR)

For U_AKIR, the ON vs OFF difference is also clear and persists over time ($p < 0.001$). We noticed here, as for U_GLOBAL, a threshold

effect with better U_AKIR scores after the tenth month ($p < 0.001$) (Figure 3).

The Subscore Relating to Axial Signs (U_AXIAL)

Concerning the U_AXIAL sub-score, the difference ON vs OFF exists and persists in the time interval studied ($p < 0.001$). Finally, no threshold effect was found at 10 months ($p = 0.83$) (Figure 4).

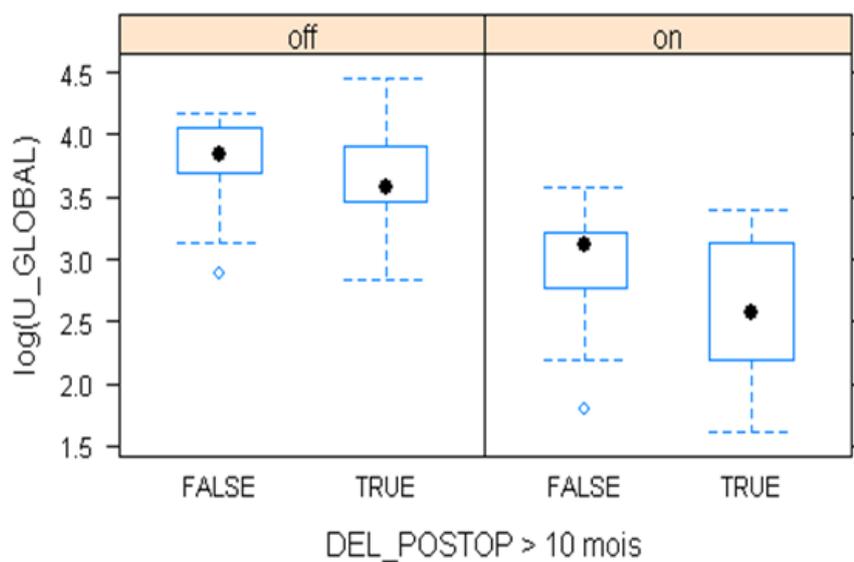


Figure 2: Temporal evolution of U_GLOBAL during the post-operative period (False: post-operative period less than 10 months; True: post-operative period greater than 10 months; DEL_POSTOP: post-operative period).

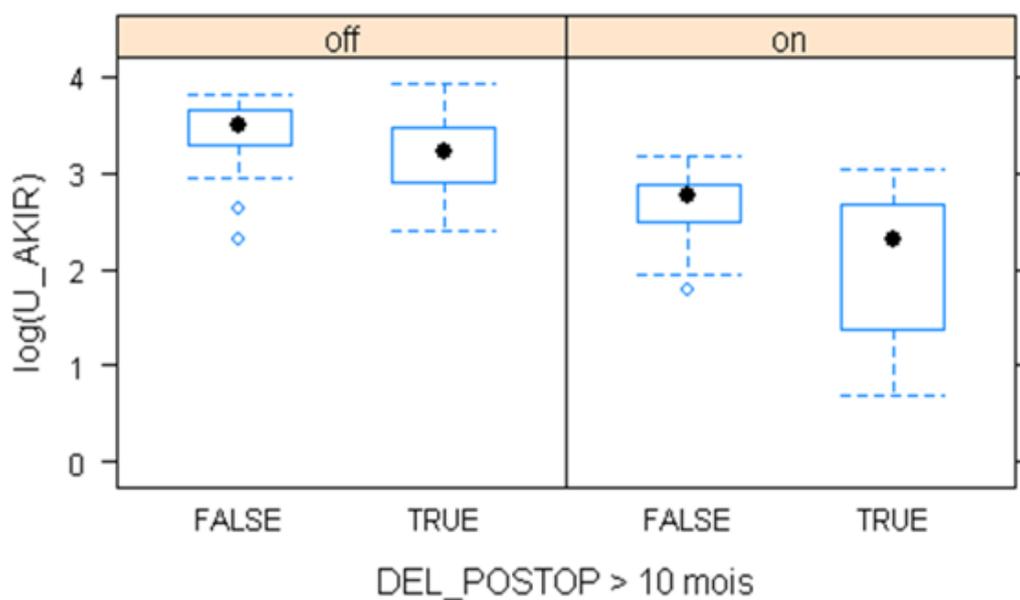


Figure 3: Temporal evolution of U_AKIR during the postoperative period (False: postoperative period less than 10 months; True: postoperative period greater than 10 months; DEL_POSTOP: postoperative period).

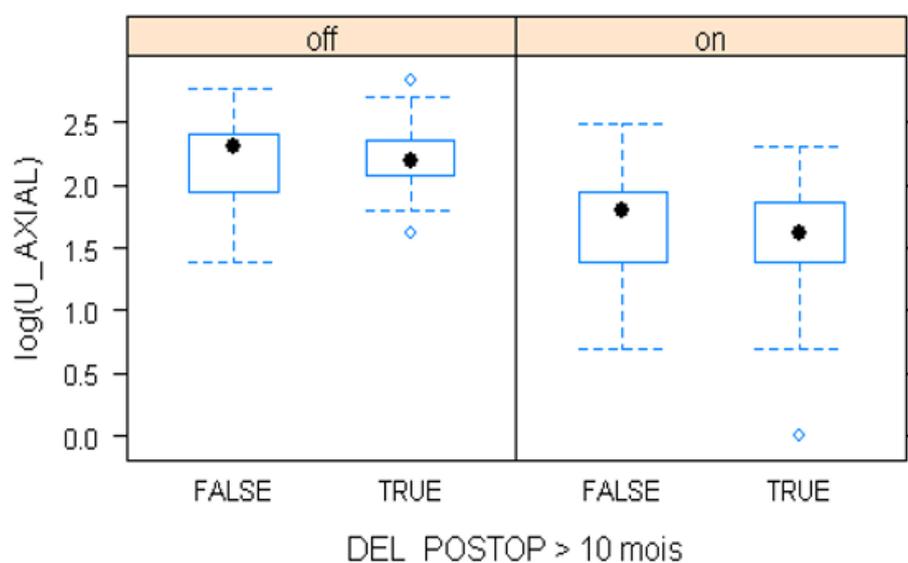


Figure 4: Temporal evolution of U_AXIAL during the postoperative period (False: postoperative period less than 10 months; True: postoperative period greater than 10 months; DEL_POSTOP: postoperative period).

Discussion

Stimulation of the subthalamic nucleus statistically significantly improves the UPDRS global motor score. This tends to confirm that it is a technique that is effective on the motor signs of Parkinson's disease. Indeed, this efficiency has already been underlined by several works [4,5]. Our results also showed that the UPDRS global motor score results were much better after 10 months with a statistically significant difference $p < 0.01$. This threshold effect at 10 months could be interpreted as the time required after the intervention for the patient to fully recover from the surgical procedure, but also for the clinician to reach optimal stimulation parameters. Some authors have estimated that a delay of 3 to 6 months could be necessary for a highly qualified clinician to achieve optimal results [6]. Beyond the clinician's experience, other parameters such as the clinical situation of each patient, the early implementation or not of neurostimulation could be taken into account in the efficiency and duration of the results [7].

U_AKIR behaved globally similar to U_GLOBAL with, on the one hand, a statistically significant and persistent ON vs OFF STIM difference over the time interval studied ($p < 0.001$) and, on the other hand, a threshold effect with much better and statistically significant results after 10 months ($p < 0.001$). These data therefore seem to support the certain effectiveness of stimulation of the subthalamic nucleus on the akineto-rigid signs of Parkinson's disease. Again, other studies have already reported such efficacy [6,8,9].

Finally, concerning U_AXIAL, even if the difference ON vs OFF STIM was statistically significant and persistent over the time interval studied ($p < 0.001$), it was not found here, contrary to the level of the two previous parameters, a threshold effect. In other words, the results before and after 10 months were not statistically

significantly different. This "ambiguous" behavior, one might say, of U_AXIAL should be attributed to a lesser and mixed efficacy in general of stimulation of the subthamic nucleus on the axial signs of Parkinson's disease. It is indeed known that axial signs (related to disorders such as gait, speech and balance, for example) respond less well to neurostimulation of the subthalamic nucleus [10,11,12]. The ON vs OFF STIM effect was persistent over the entire time interval studied, i.e. 100 months (just over 8 years), suggesting a lasting effectiveness of neurostimulation on the parameters studied. Another study on the long-term efficacy of neurostimulation, but this time focusing on isolated dystonia, also showed a robust and persistent effect of the technique over an average of about 8 years [13].

Conclusion

The effect of stimulation of the subthalamic nucleus on the clinical signs of Parkinson's disease seems to be real and persistent over the time interval studied. The results also seem much better from the 10th month. This time threshold would represent the time necessary for patients to recover well from the intervention and to benefit, after several adjustments, from optimal stimulation parameters. These are hypotheses that will have to be analyzed in the light of further studies.

Acknowledgement

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Conflict of Interest

The authors declare that they have no conflict of interest in relation to this work.

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