**SLEEP DISTURBANCES ARE MAINLY IMPROVED BY DEEP BRAIN STIMULATION OF THE SUBTHALAMIC NUCLEUS**

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We read with interest the article by Dafsari et al., which reported the effect of Deep Brain Stimulation of the Subthalamic Nucleus (STN-DBS) on non-motor symptoms (NMS) in 67 patients with Parkinson’s disease (PD) enrolled from 3 DBS centres1. They showed a clear improvement of NMS at 5-month follow-up, with partial decrement at 24-month assessment. Quality of life did not differ between baseline and 24-month follow-up.

We conducted a single-centre longitudinal study on the effect of bilateral STN-DBS on NMS in PD over a 2-year follow-up (at 6, 12 and 24 months: T6, T12, T24). Specific questionnaires for sleep and psychiatric symptoms were employed. Evaluations were completed before (T0) and after DBS on 18 consecutive patients (10 males; mean age 49.6±7.6 years; disease duration 11.4±3.6 years) undergoing STN-DBS at University of Messina (Details on study methods in Supplementary Material).

NMSS total score, PDSS-II, SCOPA-PC and PDQ-39 improved over 24 months follow-up compared to baseline (table). The effects of DBS on NMS was driven by improvement of sleep and miscellaneous domains. The effect on sleep was significant at T6, T12, T24 and was also supported by a parallel significant reduction of PDSS-2 score. PDQ39 was significantly reduced at T6 and T12 but not at T24.

A significant positive correlation by Spearman-rank test was found between the relative change of PDSS-II at T6 and the relative change of D-Ag LEDD at T6 (rho=-0.49, p=0.04). Multiple regression analysis demonstrated no association between PDQ-39 and NMSS, PDSS-2, SCOPA-PC and D-Ag LEDD at T6, T12 and T24, except for a significant association with PDSS-2 at T6 (p=0.04) and NMSS at T24.

Our data confirm that the improvement of NMS after DBS progressively decline over time at 2-year, as shown by the recent study by Dafsari et al1. Here, we suggest by using a specific questionnaire for sleep that the effect on NMS may be driven by the modulation of sleep disturbances up to 24-month follow-up.

The mechanism through which STN-DBS affects NMS might be explained by a combination of multiple mechanisms such as the effect of stimulation itself, the reduction of dopaminergic drugs and disease progression. Interestingly, in our study, improvement of sleep was correlated to D-Ag reduction at 6-month follow-up, a finding which may be in contrast with RCT studies showing a reduction of PDSS-2 under treatment with rotigotine2. However, a recent study on drug-naïve PD showed 50% increase in the frequency of insomnia associated with the use of D-ag after therapy initiation3. Moreover, in the SCOPA-PROPARK cohort including 412 patients with long PD duration, higher D-Ag dose and sleep medication use was independently associated to severe insomnia. This discrepancy might be explained by the heterogenous causes accounting for sleep disorder in advanced PD, including sleep fragmentation, restless legs syndrome, nocturia, and nocturnal pain. Our data confirm the findings of Dafsari and collaborators1, 4 and add new insights on possible mechanisms explaining sleep improvement after DBS, which should be explored in larger cohorts by polysomnographic assessment and correlation with concomitant dopaminergic and sleep medication.

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