

# Benefit of Apomorphine Infusion in a Refractory Restless Legs Syndrome

Carcangiu R (1), Staner L (1), Sellal F (2), Gaultier C (2), Duval F(3)

(1) Unité des rythmes veille sommeil, CH Rouffach (2) Département de Neurologie, Hopitaux Civils de Colmar  
(3) Psychiatrie, CH Rouffach

## INTRODUCTION

Apomorphine is a combined opioidergic and dopaminergic agonist that has been shown effective in a few reports that investigate its acute effect on small samples of patients with Restless Legs Syndrome (RLS). The present case report describes its chronic (9-month) effect on a patient affected by Parkinson's disease and severe RLS.

## METHODS

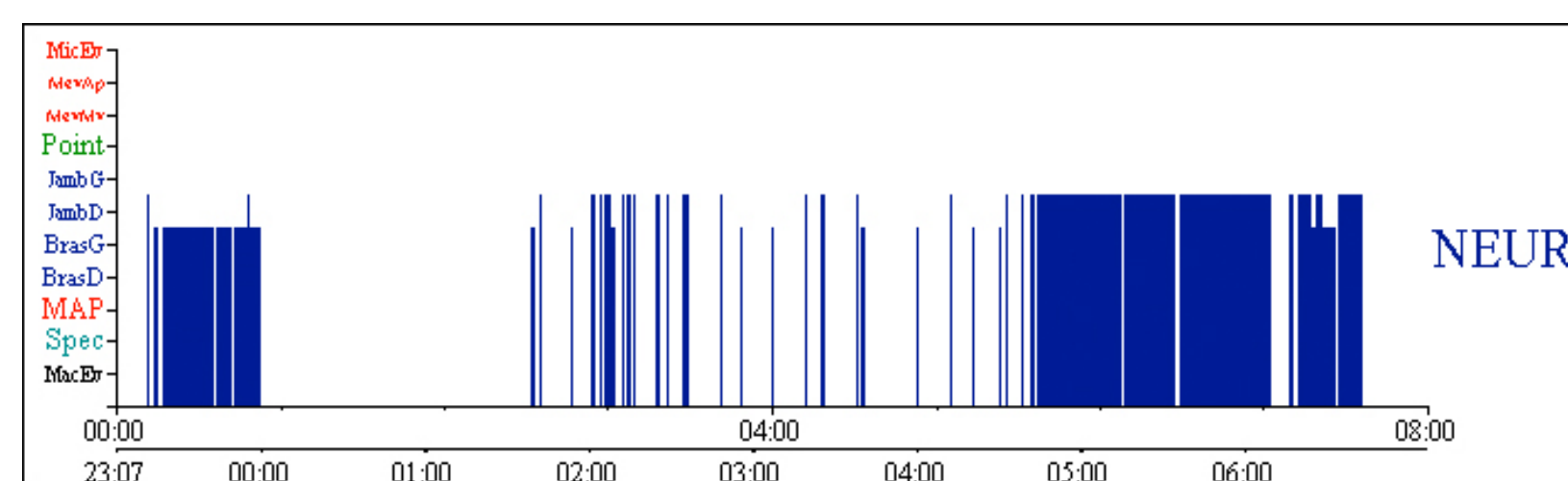
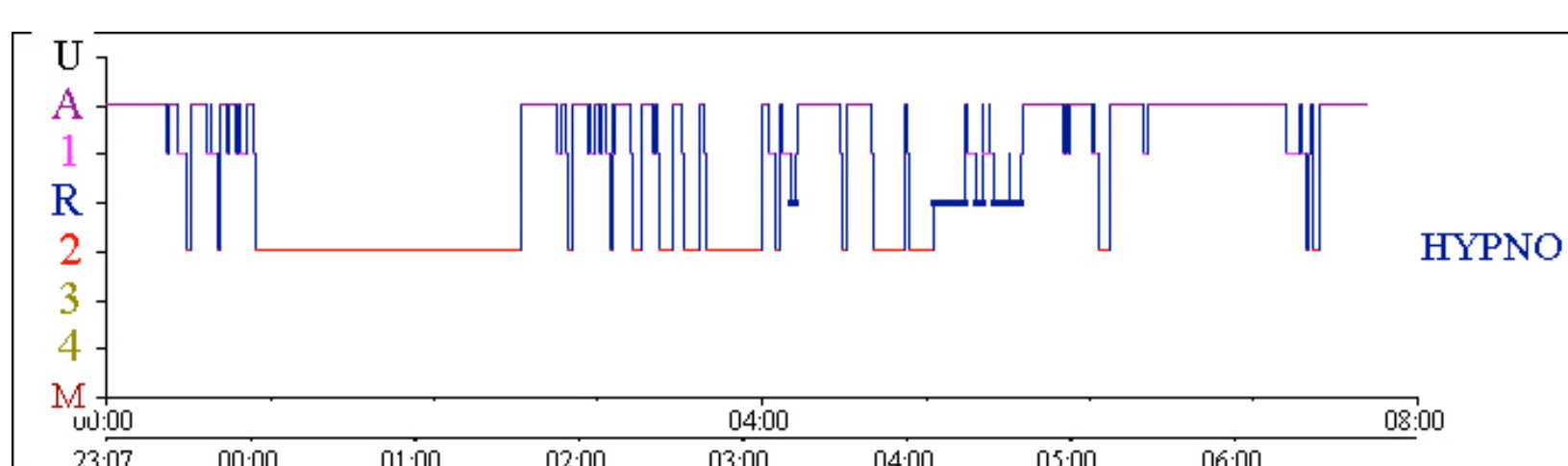
In this study, the effect of a continuous subcutaneous apomorphine infusion 9-month treatment were prospectively assessed in a male patient aged 57 years having severe RLS comorbid with a Parkinson's disease (PD). During the last ten years, this patient was followed by one of us for both diseases that were clinically well documented, including with repeated polysomnography (PSG).

## RESULTS

### a) Retrospective analysis of the follow-up before apomorphine infusion

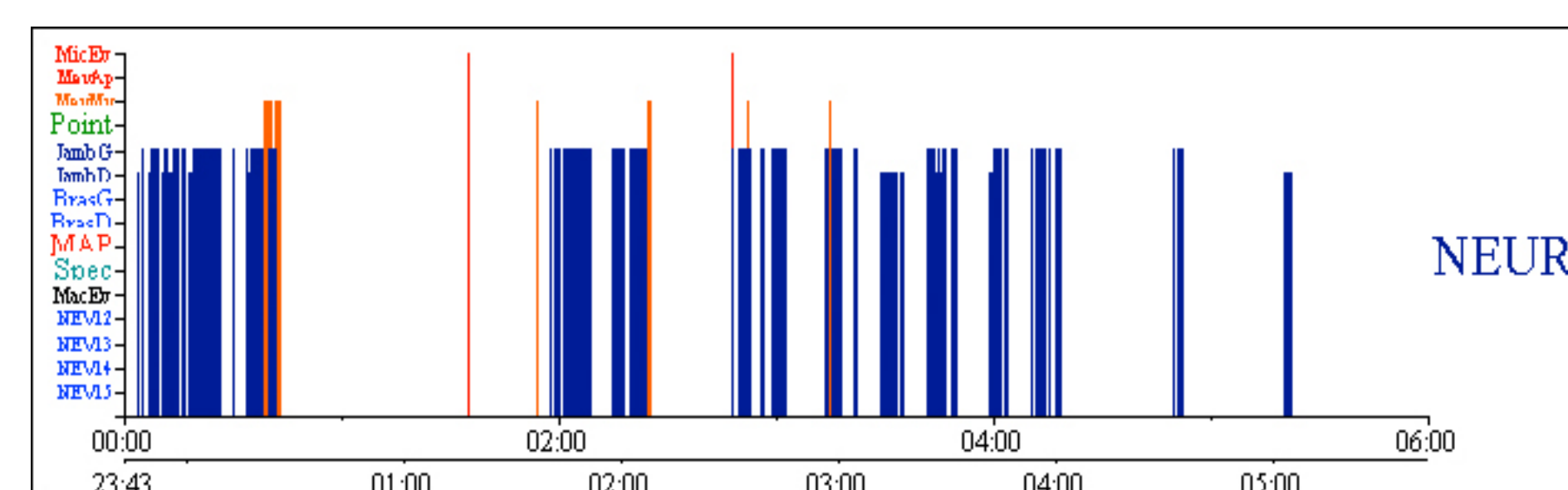
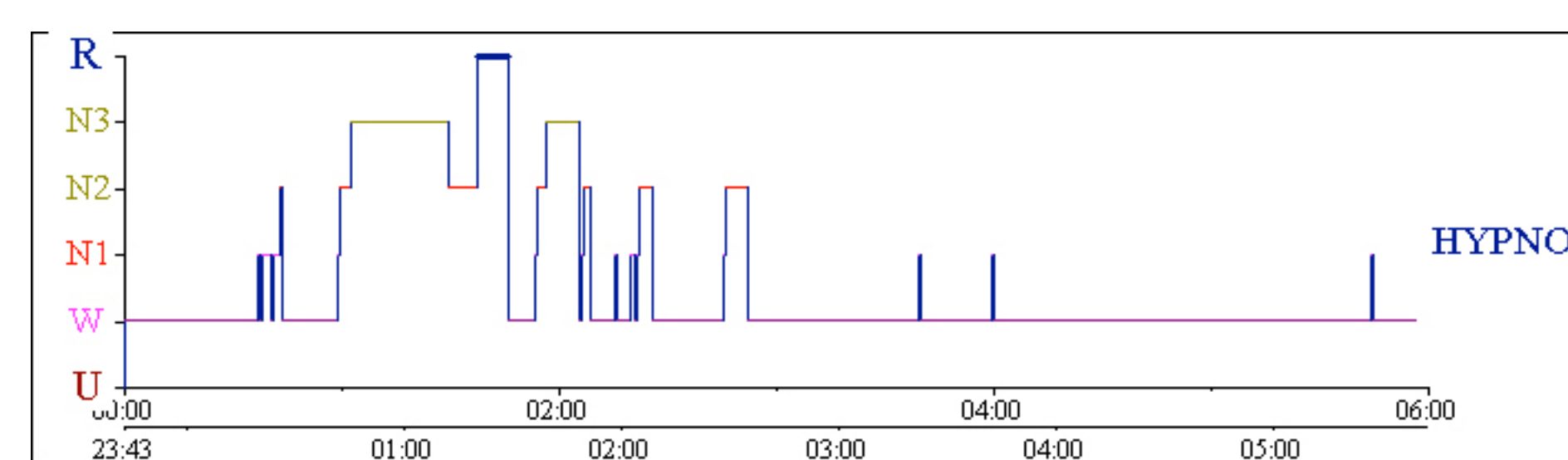
> At the age of 47 : the patient first consulted for a severe insomnia and RLS.  
> At the age of 48 : PD was diagnosed and L-DOPA therapy started.

During the 10 year follow-up the patient underwent 6 repeated PSG assessments at different times that confirmed the severity of RLS (sometimes associated with periodic leg movements of sleep) and insomnia. Numerous treatments were tried including various dopamine agonists, anti-epileptic drugs, opioids, and benzodiazepines. An iron deficiency was excluded at several times.



PSG performed when patient was 50 years old and treated by Ropinirole 1 mg/day, Clonazepam 1 mg/day and L-Dopa LP 200 mgx4/day.

The International Restless Legs Syndrome Rating Scale scored 32/40.  
Total sleep time: 246 m; sleep efficiency 58%; Slow waves sleep: 0%  
Periodic limb movement index during wakefulness 119/h (and 20/h during sleep)



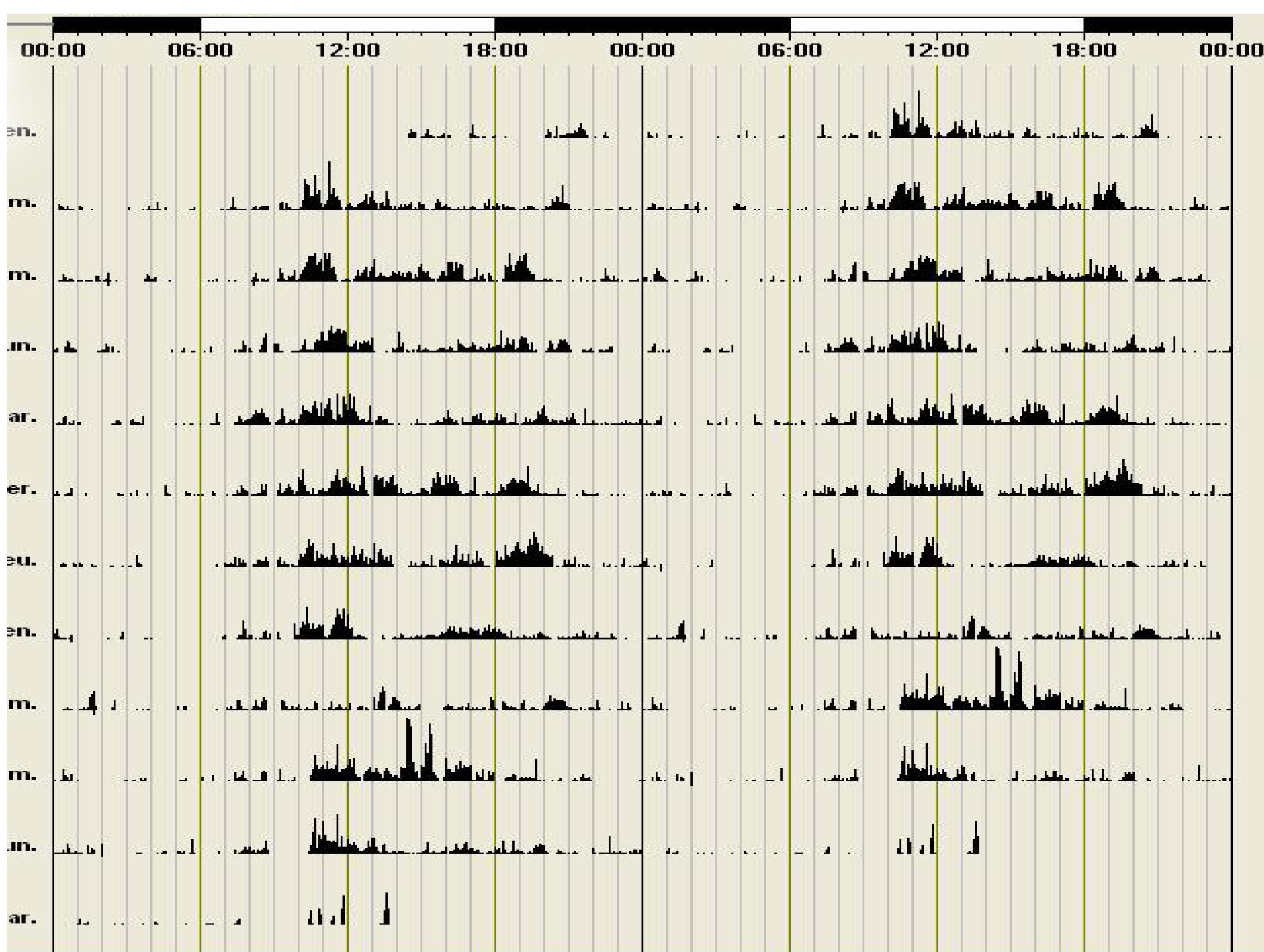
PSG performed when patient was 56 years old, the latest PSG before apomorphine infusion

Patient was treated by Rotigotine patch 6 mg/day, L-DOPA LP 175 mg x5/day; Amantadine 200 mg/day  
Total sleep time : 81 m; sleep efficiency 23%; Slow wave sleep 44%  
Periodic limb movement index during wakefulness 37/h (and 40/h during sleep)

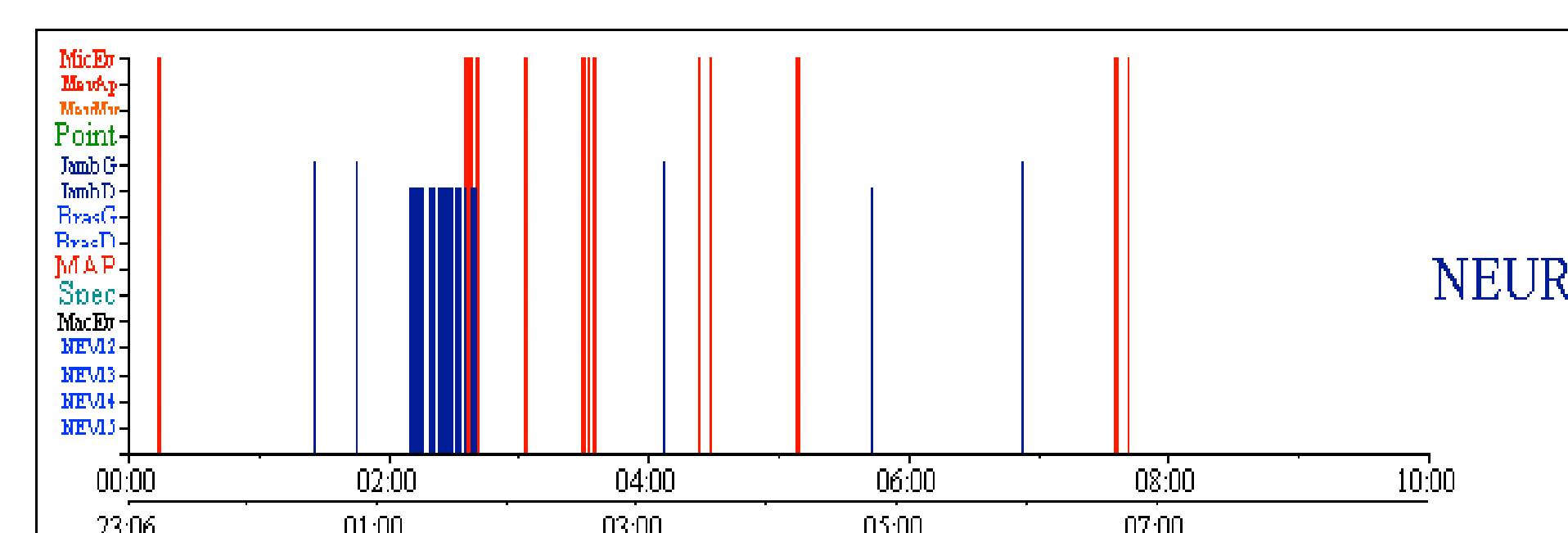
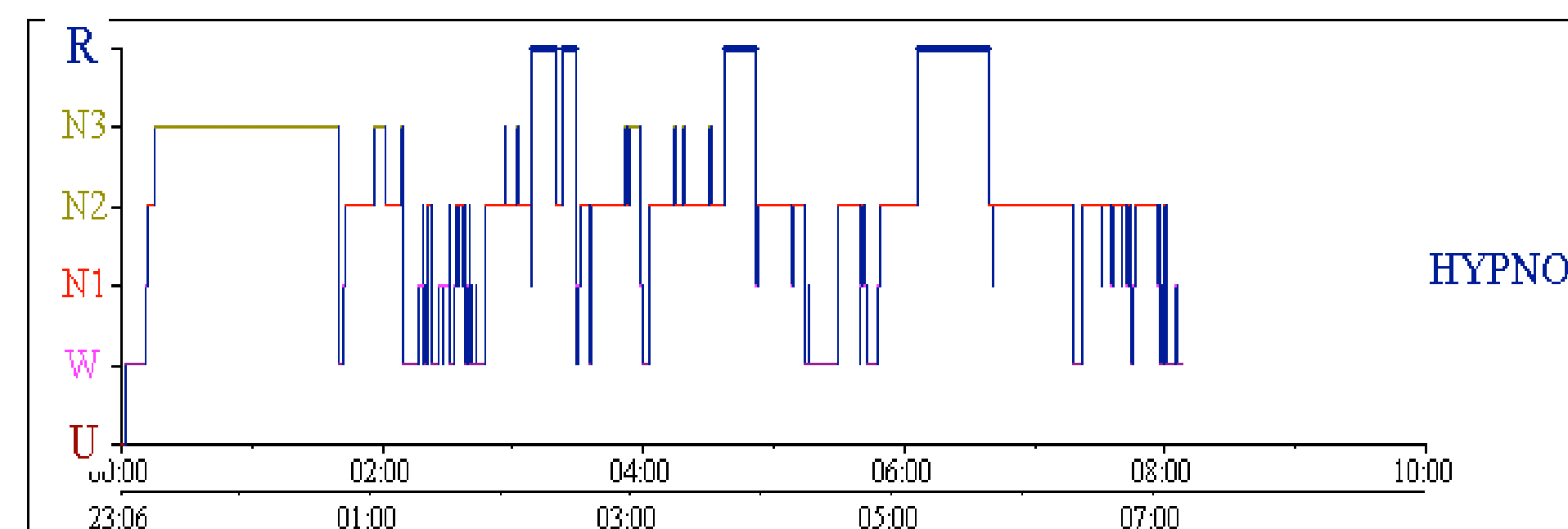
> At the age of 57: the patient showed severe PD with important motor fluctuations despite 725 mg levodopa equivalent daily dose (+ 5 mg of Ropinirole) and a continuous subcutaneous apomorphine infusion treatment was started (220 mg/24h).

### b) Prospective follow-up during the 9 month apomorphine infusion treatment

The patient reported an immediate relief of subjective RLS but no improvement on motor disabilities. These effects were sustained during the 9-month follow-up period and documented by scores on questionnaires: The International Restless Legs Syndrome Rating Scale was completed after 4, 6 and 9 months: it scored 0 /40 at each time.  
The Insomnia Severity Index was completed after 4,6 and 9 months: it scored 0-3/28



Actigraphy after 6 months of apomorphine infusion treatment showed a regular wake and sleep rhythm during 10 days : Mean sleep time 6h10; sleep efficiency 89%; sleep latency 10 mn.



PSG after 9 months of apomorphine : Total sleep time 418 m, sleep efficiency 86%, Slow wave sleep 24%  
Periodic limb movement index during wakefulness 28/h (and 3/h during sleep)

### C) Apomorphine withdrawal

After 9 months of treatment by apomorphine infusion the patient asked to stop it transiently because of subcutaneous nodules at the injection sites. He started again the same oral therapy that he had before apomorphine infusion. He complained immediately of reappearance of severe RLS and insomnia. After 6 weeks of oral therapy the International Restless Legs Syndrome Rating Scale scored 28/40 and the Insomnia Severity Index 24/28.

## CONCLUSION

Apomorphine infusion may be an effective treatment for refractory RLS in PD.