REMeDio: a proof-of-concept study of neuroprotection in REM sleep behavior disorder. Preliminary data.

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Background

-REM sleep behavior disorder (RBD) could be a **preclinical** manifestation of 'α-synucleinopaties', especially Parkinson's disease (PD).
-When PD patients present motor symptoms, about 50% of substantia nigra neurons has already been lost, indicating that the **neurodegenerative** process began years before.
-The **dopaminergic** system in idiopathic RBD (iRBD) patients is often impaired.
-Thus, iRBD patients are ideal candidates for **neuroprotective** trials, allowing early intervention before advanced neurodegeneration occurs.
-**Selegiline** is an inhibitor of monoamine oxidase B with neuroprotective effect in cellular and animal models of PD. In humans, selegiline delays the onset of disability requiring levodopa in early PD, and slowing down of PD progression has been reported (Olanow CW et al. 1995; Shoulson I 1998).

REMeDio is a 'proof-of-concept' study aimed to evaluate the feasibility of a multidimension approach to evaluate the putative neuroprotective effect of selegiline in a group of iRBD patients.

-**Study Duration:** two years per patient, with a 6-mo clinical follow-up program A further ^{123}I-FP-CIT SPECT is previewed 4 years after baseline.
-**Study Population:** The target recruitment number is 30 iRBD patients, randomly assigned to receive either selegiline and symptomatic treatment (15 pts; selegiline group) or symptomatic treatment only (15 pts; control group). The main inclusion criterion is the diagnosis of iRBD, according to current criteria.
-**Methodology**:

▪*Baseline evaluation*:
-Video-polisomnography
-^{123}I-FP-CIT SPECT
-high-density (64ch) EEG
-olfactory test
-neuropsychological assessment
-brain MRI imaging.

▪*Two years follow-up evaluation*:
-^{123}I-FP-CIT SPECT,
-high-density (64ch) EEG,
-olfactory test,
-neuropsychological assessment.

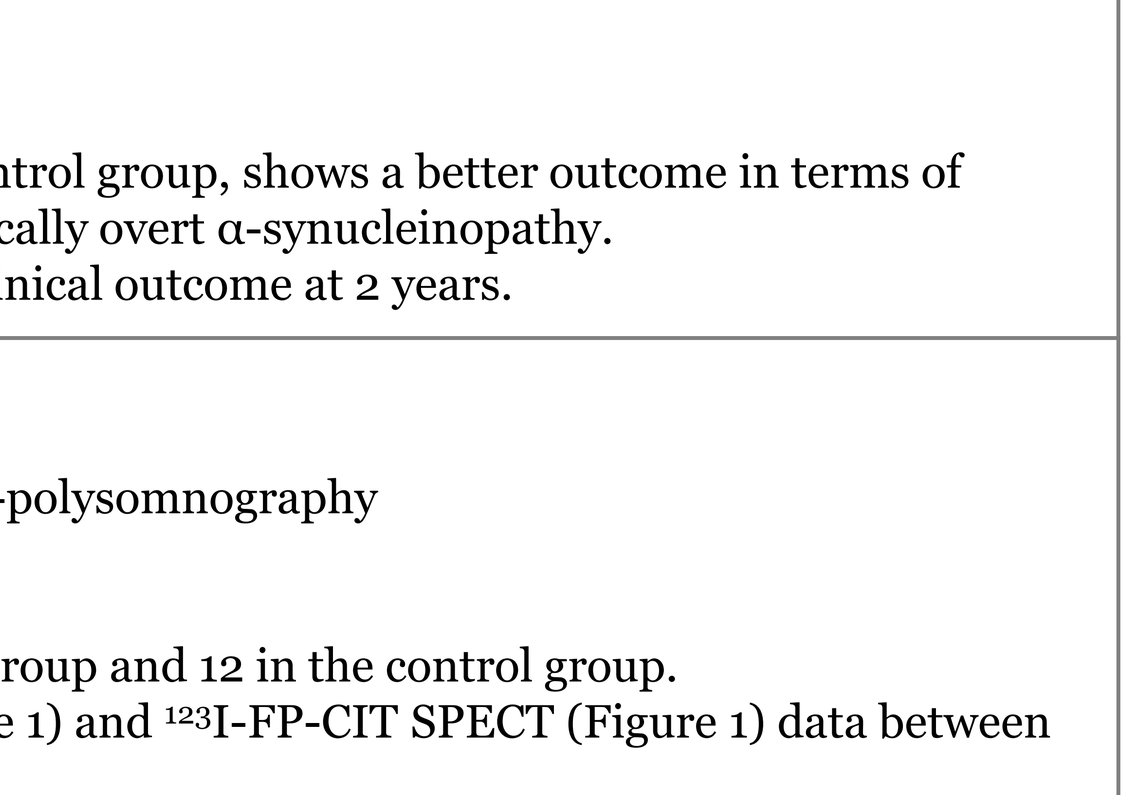
-**Objectives**:
-*Primary*: to verify whether the selegiline group, compared to control group, shows a better outcome in terms of nigro-striatal dopaminergic dysfunction and conversion to a clinically overt α-synucleinopathy.
-*Secondary*: to identify the baseline parameters able to predict clinical outcome at 2 years.

Interim Results:

➢**45 subjects** have been screened to date
✓In 6 subjects the diagnosis of iRBD was not confirmed by video-polysomnography
✓7 patients withdrew the study
✓6 patients are performing baseline evaluations,
✓**26 patients** have currently been enrolled, 14 in the selegiline group and 12 in the control group.
❑ There are no significant differences in baseline clinical (Table 1) and ^{123}I-FP-CIT SPECT (Figure 1) data between the two groups.
❑ 11 patients (7 in control group and 4 in selegiline group) completed the 2-y follow-up assessment.
❑ Three of them converted to PD and they were all in the control group.

Table 1	Controls	Selegiline	p value
n	12	14	
Gender, M-F	10 – 2	14 – 0	n.s.
Age, y	66.7±8.9	66±7.5	n.s.
MMSE	28.7±1.6	29.3±0.8	n.s.
Beck Depression Inventory-II	10.7±10.1	14.9±10.6	n.s.
Olfactory test (norm ≥ 6)	5.2±1.4	5.3±1.0	n.s.

Figure 1



Conclusion:
These very preliminary data on an ongoing study shows that assessing the conversion rate and nigrostriatal function in iRBD patients receiving a putative neuroprotective drug is feasible in a clinical research setting.

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