D.3.5 REM sleep disorder behaviour

Bibliographic reference	Di,Giacopo R., Fasano,A., Quaranta,D., Della,Marca G., Bove,F., Bentivoglio,A.R., 20120808, Rivastigmine as alternative treatment for refractory REM behaviour disorder in Parkinson's disease, Movement Disorders, 27, 559-561, 2012
Country/ies where the study was carried out	Italy
Study type	RCT
Aim of the study	To assess the efficacy of rivastigmine to treat RBD in whom conventional therapy has failed (melatonin or clonazepam)
Study dates	July 2011 received. Published Dec 2011
Source of funding	None reported.
Sample size	n = 12
Inclusion criteria	Consecutive patients with idiopathic PD and RBD refractory to melatonin (up to 5mg per day) and clonazepam (up to 2 mg per day). RBD confirmed by polysomnography without atonia (RSWA) features
Exclusion criteria	Dementia, orthostatic hypotension, chronic obstructive pulmonary diseases, active peptic ulcer epilepsy, urinary obstruction, cardiac arrhythmias, treatment with anticholinergics or antidepressants, and DBS
Details	Before randomization all patients underwent clinical interview, neuro exam, neuropsychological examination, psychiatric assessment, blood pressure measured, and electrocardiogram. RBD frequency at baseline assessed on basis of 1 month diary of patients RBD episodes filled in by the bed partners Patients considered affected by severe RBD if suffered> 5 episodes a week. Each patient randomized to receive either rivastigmine patch 4.6mg per day or a placebo patch for 3 weeks washout period of 7 days, each group shifted to other treatment for an additional 3 weeks antiparkinsonian therapy maintained unaltered for the duration of study

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Interventions	Each patient randomized to receive either rivastigmine patch 4.6mg per day or a placebo patch for 3 weeks washout period of 7 days, each group shifted to other treatment for an additional 3 weeks
Results	11 men, 1 female Mean age 67.7 (7.3); disease duration 9.2 (3.2) Mean LDD = 445.8 mg Adverse events 2 patients dropped out because of orthostatic hypotension and asthenia, both occurring during active treatment arm RBD episodes RBD episodes significantly less frequent in rivastigmine treatment compared to baseline (Z = -2.524, p = 0.012); not the case in placebo (Z= -1.289, p=.197) Mean frequency of RBD episode significantly lower in rivastigmine compared with placebo (Z=-2.207, p=0.027). Median *(25th - 75th percentiles)= 2.5 (0.0 to 4.5) Reduction in frequency of RBD episodes was more consistent in patients with severe RBD.
Overall Risk of Bias	NICE RCT checklist: 1. An appropriate method of randomization was used to allocate pts to treatment groups? Unclear - details on randomization method not given 2. There was adequate concealment of allocation: details for allocation concealment details not given 3. The groups were comparable at baseline, including all major confounding and prognostic factors? cross over trial. Random allocated treatment order groups were comparable 4. Comparison groups received same care apart from interventions: yes 5. Pts receiving care were kept blind to tmt allocation: No details given on blinding 6. Individuals administering care were kept blind to tmt allocation: No details given on blinding 7. All groups followed up for an equal length of time: yes - equal time follow-up 8. Groups comparable for treatment completion? No - 2 patients dropped out of rivastigmine group, no drop out from placebo 9. Groups were comparable with respect to availability of outcome data? Data for 2 patients was not available for the placebo trial. 10. Study had appropriate length of follow up? Unclear whether 3 weeks is adequate 11. Study used a precise definition of outcome: No; primary outcome was measured by bedpartner diary on RBD episodes. No other measure used i.e. polysomnography 12. Valid and reliable method was used to determine the outcome: No; primary outcome was measured by bedpartner diary on RBD episodes. 13. Investigators were kept blind to participants' exposure to the intervention: unclear - details for blinding were not given 14. Investigators were kept blind to other important confounding and prognostic factors: Unclear - details for blinding of prognostic factors were not given. overall quality = LOW (risk of bias = high)

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Other information	None