Clinical Characteristics of Park Sleep: excessive daytime sleepiness subtype in Parkinson's disease.

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OBJECTIVE

- To define the clinical characteristics of the Park Sleep subtype with Excessive Daytime Sleepiness (EDS) using a single factor, matched group, prospective observational study.

BACKGROUND

- Recently, non-motor symptoms (NMS) dominant subtypes within Parkinson's disease (PD) have been proposed and Park Sleep appears to be a specific endophenotype with patients expressing EDS, rapid eye movement behaviour disorder (RBD) or both[1,2].
- The clinical and imaging biomarkers of this endophenotype are unclear.

METHODS

- In this prospective observational study, we have used EDS (measured by Epworth Sleepiness Scale (ESS) after exclusion of known secondary causes of EDS) as the single factor to differentiate Park Sleep EDS (PD-EDS) (ESS>11) versus non-EDS (PD-nonEDS) (ESS ≤11) and prospectively studied subjects matched for age, PD age at onset and sex.
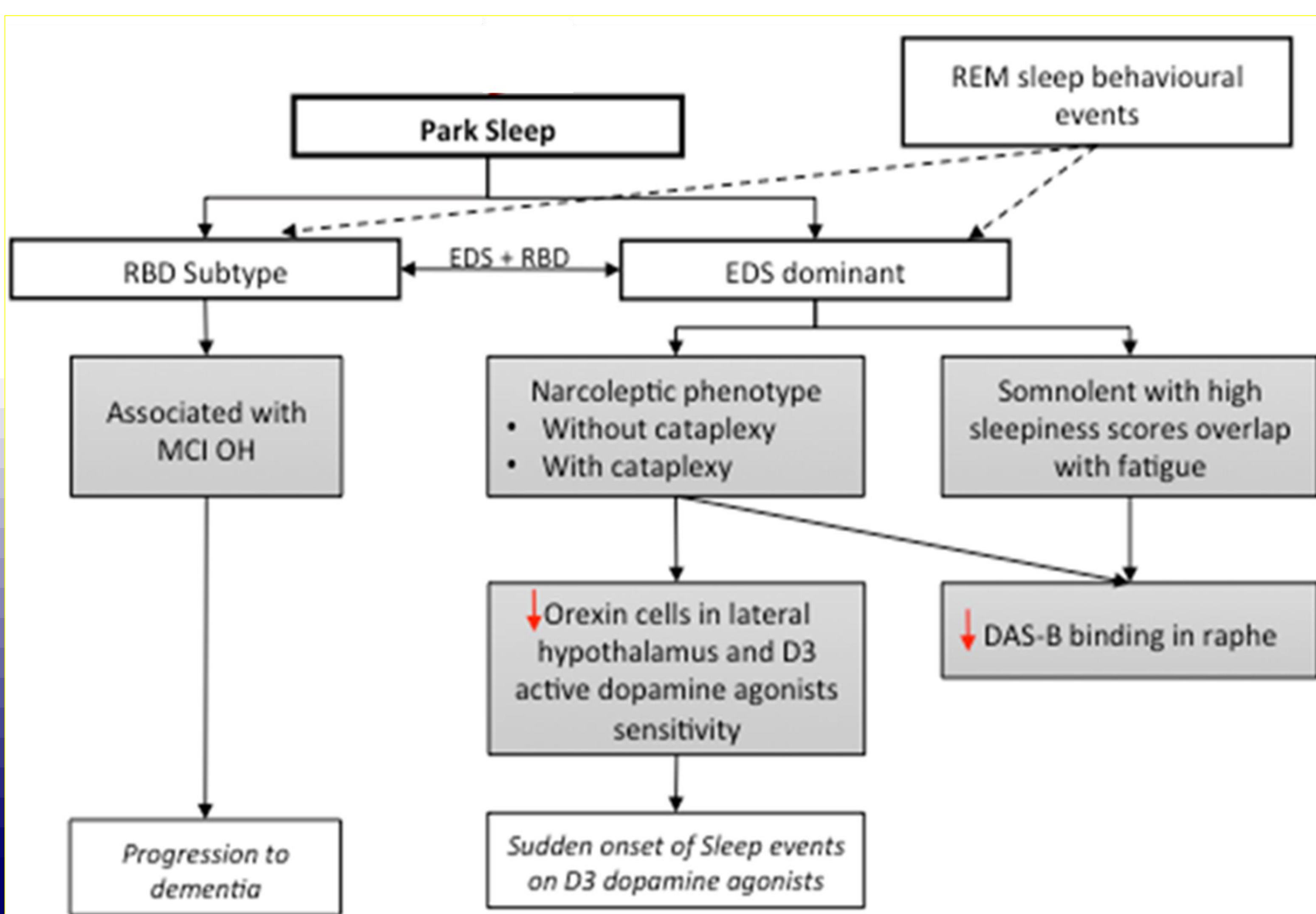
Table 1 Demographics and clinical characteristics

Table 1 Demographics and clinical characteristics	PD-nonEDS (N=318)	PD-EDS (N=104)	p-value
Mean age in years (SD)	65.85 (11.96)	67.35 (10.46)	0.45[1]
Male in %	63.5	67.3	0.48[2]
Mean PD onset in years (SD)	60.92 (12.61)	60.83 (11.75)	0.76[1]
Mean disease duration in years (SD)	4.90 (5.20)	6.42 (6.09)	0.014[1]
Mean SCM-Motor total (SD)	16.15 (8.62)	21.74 (9.89)	< 0.0001[1]
Mean MMSE total (SD)	28.65 (2.09)	27.96 (2.75)	0.014[1]
Median HY (Range)	2 (0-5)	3 (1-5)	< 0.001[2]
Mean physical fatigue (SD)	36.48 (25.88)	50.74 (21.87)	< 0.0001[1]
Mean mental fatigue (SD)	30.76 (26.30)	43.66 (27.35)	< 0.0001[1]
Mean PDQ-8 Summary index (SD)	22.42 (18.02)	33.98 (19.56)	< 0.0001[1]
Mean EQ-5D Index (SD)	0.68 (0.28)	0.56 (0.29)	< 0.0001[1]
Mean EQ-5D VAS (SD)	67.67 (20.64)	58.22 (20.43)	< 0.0001[1]
Mean NMSS total (SD)	41.51 (31.28)	71.26 (42.25)	< 0.0001[1]
Mean HADS Anxiety (SD)	5.24 (4.0)	7.47 (4.60)	< 0.0001[1]
Mean HADS Depression (SD)	4.68 (3.67)	6.71 (3.61)	< 0.0001[1]
Mean PDSS (SD)	111.73 (25.09)	96.98 (25.14)	< 0.0001[1]
Mean CISI total (SD)	6.28 (3.60)	8.61 (4.01)	< 0.0001[1]

*PD-EDS with ESS >11 and PD-non EDS with ESS ≤11 [2]
[1]two-sample Wilcoxon rank-sum (Mann-Whitney) test, [2]Pearson chi2 test,
ESS = Epworth sleepiness scale, PD = Parkinson's disease, Scopa = , MMSE = Mini mental state examination, HY = Hoehn and Yahr, PDQ-8 = Parkinson's disease questionnaire – 8, EQ-5D = , VAS = visual analogue scale, NMSS = non-motor symptoms scale, HADS = Hospital Hospital Anxiety and Depression Scale, PDSS = Parkinson's disease sleep scale, CISI = Clinical impression of severity index

Table 2 Correlation of Epworth Sleepiness Scale and other assessed clinical characteristics

	ESS total*		ESS total*
Age	0.04	NMSS domain 1 Cardiovascular/ Falls	0.19
PD onset	-0.04	NMSS domain 2 Sleep/ Fatigue	**0.44**
Disease duration	0.21	NMSS domain 3 Mood/ Cognition	0.23
Scopa-Motor	0.32	NMSS domain 4 Perceptual problems	0.26
MMSE total	-0.12	NMSS domain 5 Attention/ Memory	0.32
HY	0.32	NMSS domain 6 Gastrointestinal tract	0.28
Physical fatigue	0.23	NMSS domain 7 Urinary	0.22
Mental fatigue	0.18	NMSS domain 8 Sexual function	0.12
PDQ-8 SI	0.38	NMSS domain 9 Miscellaneous	0.21
EQ-5D total	-0.29	NMSS total	**0.45**
CISI total	0.33	HADS Anxiety	0.27
PDSS total	-0.33	HADS Depression	0.30

*Spearman's rank correlation
ESS = Epworth sleepiness scale, PD = Parkinson's disease, Scopa = , MMSE = Mini mental state examination, HY = Hoehn and Yahr, PDQ-8 = Parkinson's disease questionnaire – 8, EQ-5D = , VAS = visual analogue scale, NMSS = non-motor symptoms scale, HADS = Hospital Hospital Anxiety and Depression Scale, PDSS = Parkinson's disease sleep scale, CISI = Clinical impression of severity index

CONCLUSION

- **This large scale observational multimodal biomarker driven comparative study examining the PD-EDS subtype suggests the existence of a Park sleep phenotype.**

- **The clinical implications are:**
  - ✓ **Enrich samples for clinical trials related to sleep dysfunction in PD**
  - ✓ **Provide subtype specific tailored therapy for people at risk of sudden onset of sleep**
  - ✓ **Provide driving advice for those with narcoleptic phenotype**
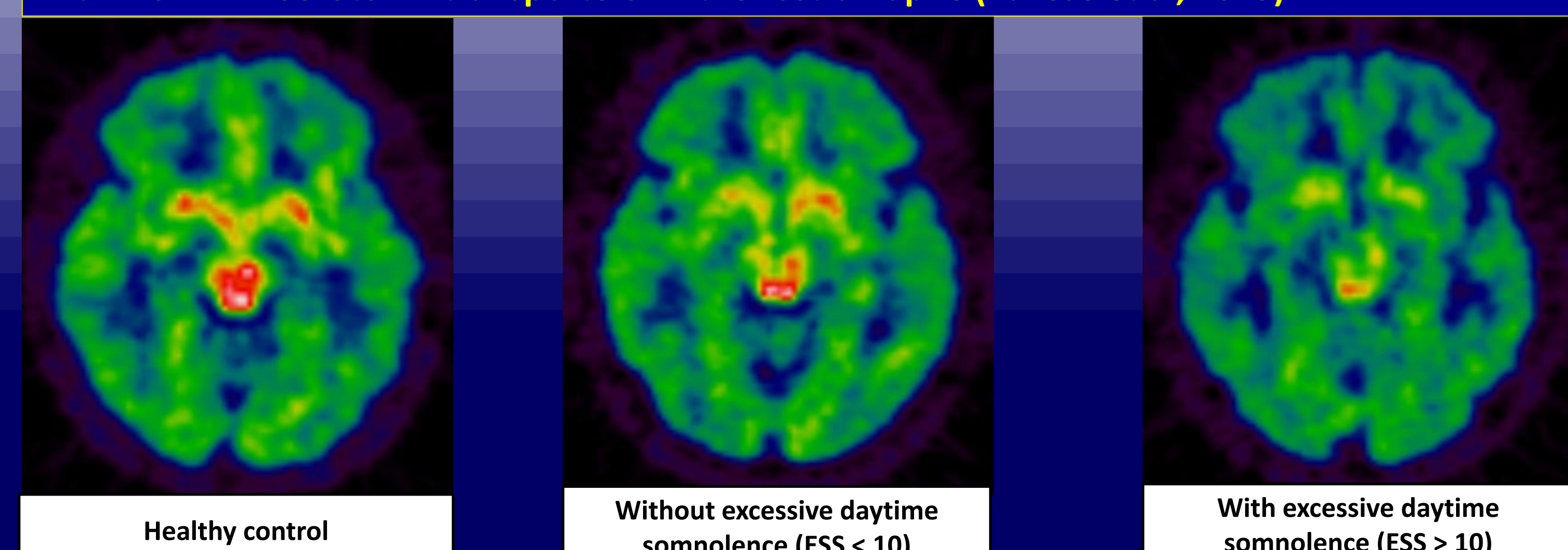 - ✓ **Provide adequate night-time protection for PD patients with physical RBD**

EDS = Excessive Daytime Sleepiness, RBD = REM sleep behaviour disorder, REM = Rapid Eye Movement, MCI = Mild Cognitive Impairment, OH = Orthostatic Hypotension

11C-DASB PET: Serotonin transporters in the rostral raphe (Pavese et al, 2013) [3]

Healthy control | Without excessive daytime somnolence (ESS < 10) | With excessive daytime somnolence (ESS > 10)

ESS = Epworth sleepiness scale

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[3]Pavese, Metta, Chaudhuri, Brooks et al, AAN 2013