



Appendix 2

**This appendix was part of the submitted manuscript and has been peer reviewed.
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Appendix to: Titova N, Chaudhuri KR. Non-motor Parkinson disease: new concepts and personalised management. *Med J Aust* 2018; 208: 404-409. doi: 10.5694/mja17.00993.

Appendix 2: The relationship of alpha-synuclein deposition and Braak stages to non-motor symptoms in Parkinson disease

Anatomical region	α -synuclein pathology	Braak Parkinson's disease stage	Nonmotor symptoms
Autonomic Nervous System			
Sympathetic ganglia	LN, LB	1-6	Autonomic: Orthostatic hypotension Postural intolerance Cardiac rhythm abnormalities
Gastroesophageal/ enteric plexus	LN, LB	1-6	Constipation Postprandial hypotension
Pelvic Plexus	LN, LB	1-6	Nocturia, impotence, urgency of urination Erectile failure
Cardiac sympathetic nerves	LN, LB	Unknown	Orthostatic hypotension
Adrenal gland	LB	1-6	Fatigue Poor exercise tolerance
Skin			
Epidermal nerves	LN	2-6	Abnormal sensitivity to pain Cutaneous hyperalgesia (allodynia)
Olfactory bulb			
Anterior olfactory nucleus (olfactory brain nuclei)	LN, LB	1	Hyposmia or anosmia
Medulla			
Dorsal motor n. vagus (parasympathetic)	LB, iLB	1	Dysautonomia (gastrointestinal tract, bladder related symptoms)
Pons			
Locus coeruleus, raphe, lateral tegmental nuclei	LB, LN	2	Depression, Anxiety Non REM parasomnias, RBD
Midbrain			
Substantia nigra	LB, LN	3	Extrapyramidal motor
Diencephalon	LB, LN	3, 4	Sleep disorders (Insomnia, Parasomnias), Weight changes
Thalamus	LB	3, 4	Pain modulation
Hypothalamus	LB	3, 4	Appetite
Basal forebrain			
Nucleus basalis Meynert	cLB	4	Executive dysfunction
Amygdala, hippocampus	cLB	4	Emotional behaviour
Neocortex			
Prefrontal cortex	cLB	5	Agnosia, Apraxia
Temporal parietal cortex	cLB	6	Dementia Psychosis
Retina	LN	Unknown	Diplopia, Reading difficulties

LB= lewy bodies; cLB = cortical LB; iLB = incidental LB; LN = lewy neurites; RBD = rapid eye movement behaviour sleep disorder

Jellinger KA. Neuropathobiology of non-motor symptoms in Parkinson disease. J Neural Transm (Vienna). 2015; 122: 1429-1440.