Phosphorilated alpha-synuclein cutaneous deposits and cardiac autonomic involvement in α-Synucleinopathies

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Introduction and objective

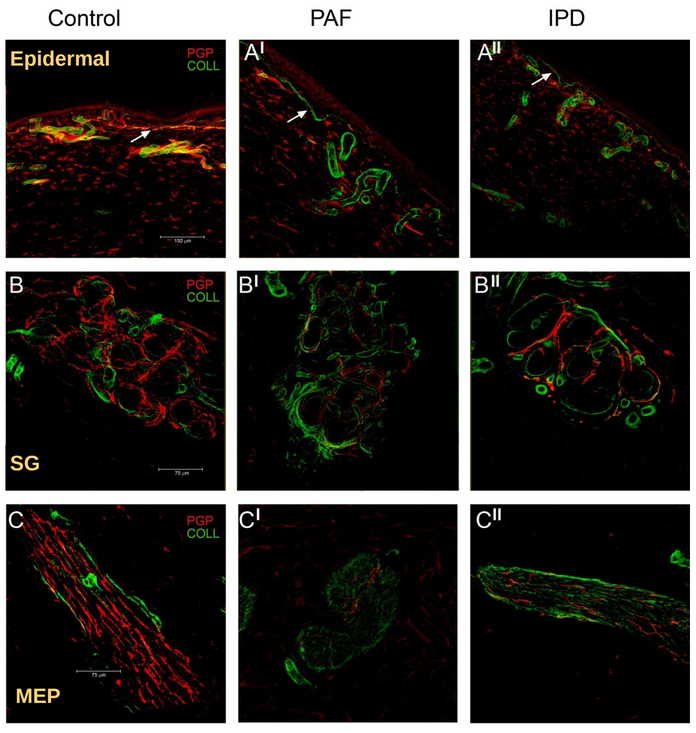
Differential diagnosis among α-Synucleinopathies, including idiopathic Parkinson's disease (iPD), dementia with Lewy bodies (DLB), pure autonomic failure (PAF) and multiple system atrophy (MSA), can be challenging in vivo. Cutaneous and cardiac autonomic denervation was reported in iPD, DLB and PAF as opposed to MSA and, recently, the detection of skin nerve phosphorylated-α-synuclein (p-α-Syn) deposits provided a marker for diagnosing and exploring the spreading of the pathology premortem [1-3]. We aimed to compare 123I-MIBG scintigraphy and skin biopsy findings in α-Synucleinopathies in order to: 1) verify the relation between myocardial and skin innervations and cutaneous p-α-Syn deposition; 2) identifying patterns of autonomic dysfunction across multiple sites in vivo.

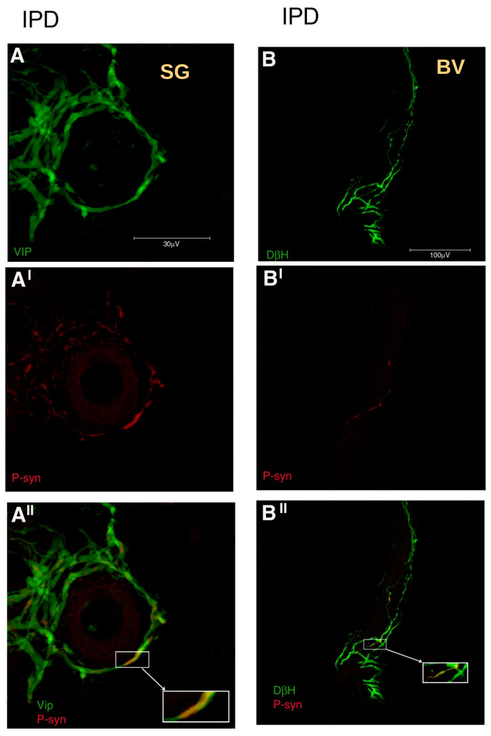
Material and methods

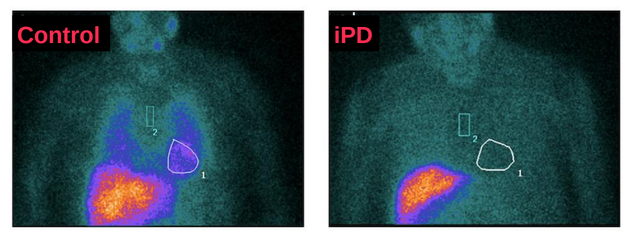
We studied 54 patients (8 DLB, 21 iPD, 13 PAF, 12 MSA) (sse table) who underwent 123I-MIBG scintigraphy and skin biopsies to evaluate skin innervation and p-α-Syn deposition [2,3].

	N.of PATIENTS (54)	SEX (M/F)	AGE	AGE at ONSET	DISEASE DURATION	H&Y STAGE
LBD	8	5/3	69.7 ± 3.3	66.6 ± 3	3.2 ± 0.7	2.28 ± 1.10
IPD	21	14/7	71.5 ± 1.6	60.1 ± 1.6	11.1 ± 1.4 *	2.14 ± 1.13
PAF	13	9/4	63.6 ± 1.8	53.61 ± 2.2	9.8 ± 1.1 *	-
MSA	12	9/3	65 ± 3	61.5 ± 3.5	3.5 ± 0.58	2.5 ± 0.72
CONTROLS	33	15/14	66.7 ± 11	-	-	-

Results







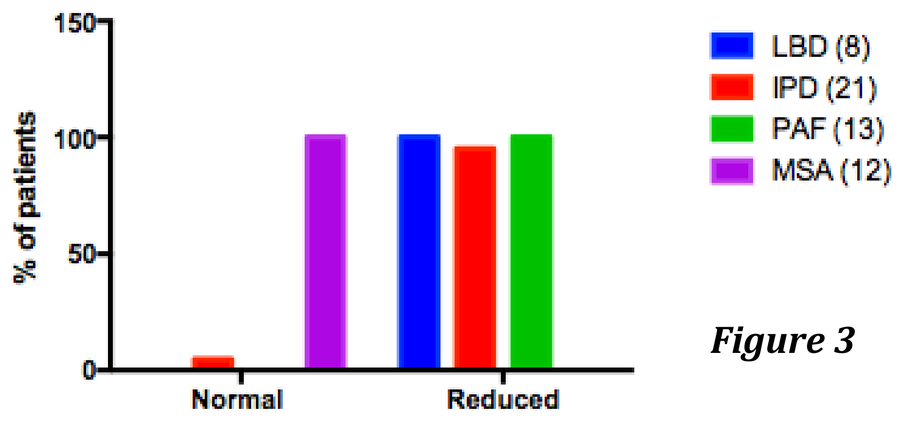


Figure 3

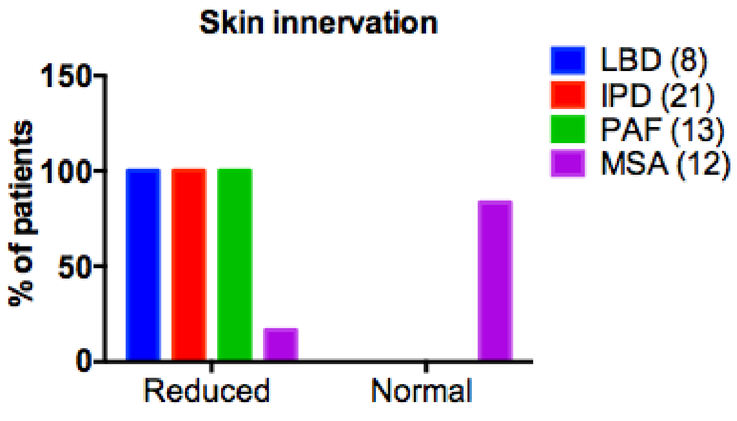


Figure 1

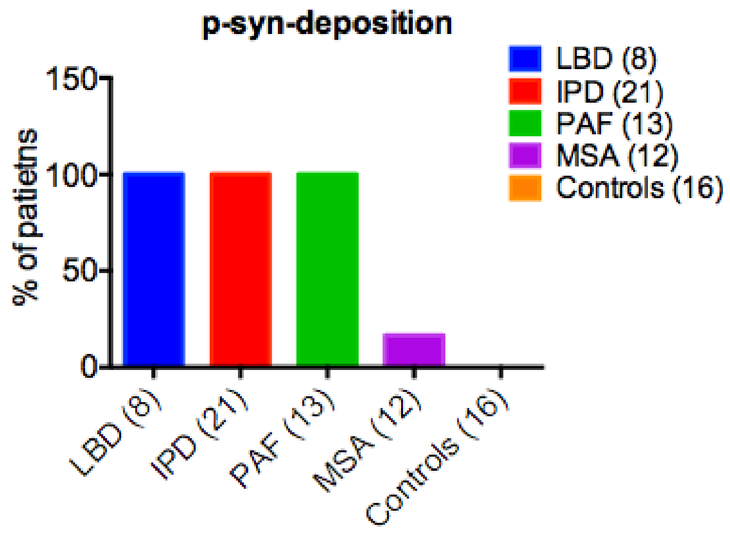


Figure 2

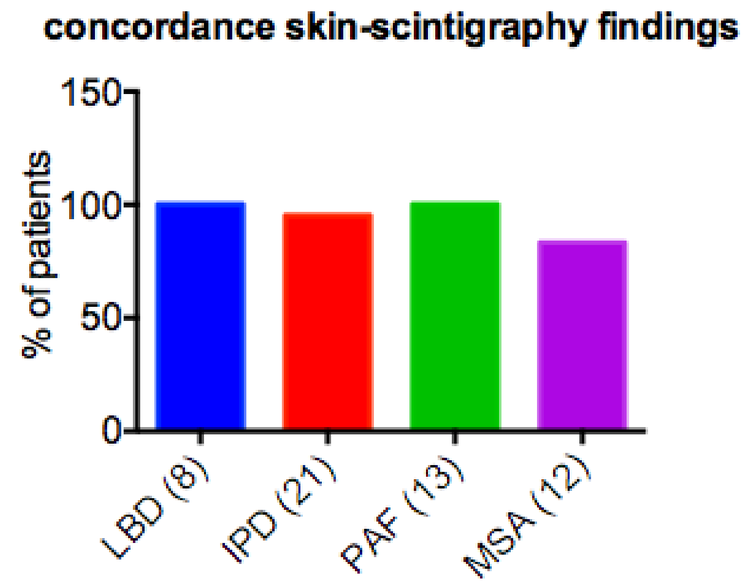


Figure 4

Skin nerve fiber loss and p-α-Syn deposits were documented in all iPD, DLB and PAF patients (figure 3) and were associated with cardiac denervation in 95% of iPD and in 100% of DLB and PAF cases respectively. Conversely, normal skin findings were observed in 84% of MSA patients whereas scintigraphy was normal in all.Concordance among MIBG scintigraphy and skin biopsy results was observed in 100% of DLB, PAF, 95% of iPD and 84% of MSA patients (Figure 4).

Conclusions

1) Skin biopsy and 123-MIBG scintigraphy can be considered alternative test for the differential diagnosis of iPD, PAF and DLB versus MSA; 2) in iPD, PAF and DLB peripheral autonomic involvement is often simultaneously widespread in different autonomic branches.

References

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