

## **Cutaneous Alpha-Synuclein Deposition in Multiple System Atrophy**

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**Objective:** To define the peripheral neural deposition of alpha-synuclein in MSA.

**Background:** We recently reported that  $\alpha$ -synuclein can be detected within cutaneous autonomic nerve fibers of patients with Parkinson's disease (PD). We now report the deposition of phosphorylated and total alpha-synuclein in patients with MSA, and compare those findings to controls and individuals with PD.

**Design/Methods:** Twenty-nine individuals with MSA, 22 individuals with PD and 10 healthy control subjects had clinical examinations, autonomic function testing and skin biopsies taken from multiple proximal and distal sites. Skin biopsies were stained for PGP9.5, phosphorylated and total  $\alpha$ -synuclein and results compared to autonomic function tests.

**Results:** Patients with MSA had evidence of peripheral phosphorylated  $\alpha$ -synuclein deposits in all subjects ( $P < 0.001$  vs controls, where no  $\alpha$ -synuclein was detected) at proximal and distal biopsy sites. Significant differences in synuclein deposition between MSA subjects and PD subjects ( $P < 0.01$ ) was noted at all biopsy sites.

### **Conclusions:**

We report the largest study of cutaneous alpha synuclein in individuals with multiple system atrophy. Contrary to expectations, peripheral deposition of phosphorylated  $\alpha$ -synuclein was present in all subjects with MSA and PD. These findings may offer insights into the different patterns of synuclein deposition across a spectrum of neurodegenerative diseases. The results carry significant implications for disease diagnosis, prognosis and therapeutic interventions that alter the natural history of the disease.