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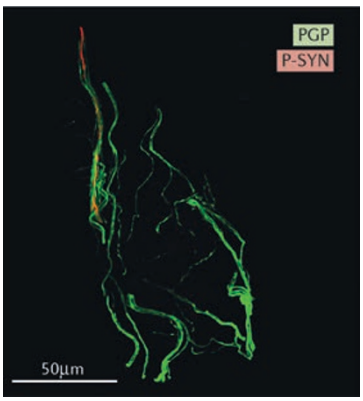
DEMENTIA

Skin α-synuclein deposits — a new biomarker for DLB?

> skin biopsy is an easy and inexpensive technique

The accurate diagnosis of dementia depends on identification of the underlying pathology, which is difficult to accomplish in living patients owing to the inaccessibility of the affected brain tissue. New research reported in *Neurology* indicates that the presence of phosphorylated α-synuclein deposits in the nerves of the skin is a distinguishing feature of dementia with Lewy bodies (DLB), and could serve as a biomarker for this condition.



Phosphorylated α-synuclein (P-SYN) deposition (red) in a skin biopsy sample from a patient with DLB. Skin nerves are visualized with an antibody against the pan-neuronal antigen PGP 9.5 (green). Image courtesy of V. Donadio.

DLB is one of the most common forms of dementia — second only to Alzheimer disease in terms of prevalence — and is characterized pathologically by aggregation of α-synuclein in the brain. Dysfunction of the autonomic nervous system is frequently reported in patients with DLB, and the skin contains an extensive network of autonomic nerve fibres that could potentially be affected by α-synuclein pathology.

Vincenzo Donadio and colleagues recruited 18 patients with DLB (11 of whom had autonomic dysfunction), 13 patients with nonsynucleinopathy dementia (NSD), and 25 healthy controls. "Skin innervation was studied in a small sample taken by skin biopsy — a minimally invasive technique requiring no suture," explains Donadio. "We used an indirect immunofluorescence technique in which the primary antibody was directed against α-synuclein phosphorylated at Ser129, which is thought to be the misfolded form of native α-synuclein."

Phosphorylated α-synuclein was detected in the skin in all the patients with DLB, but not in the patients with NSD or the healthy controls. The DLB cohort also showed evidence of small-fibre neuropathy, which was especially severe in the subset of patients with autonomic dysfunction. This latter finding suggests that α-synuclein deposits in the skin have pathogenic as well as diagnostic relevance.

The researchers acknowledge that their study has a number of limitations, including a lack of autopsy-based confirmation of the diagnosis, possible biases in patient selection, and the small number of participants."If confirmed in a larger sample of patients, our work will represent an important step forward for DLB biomarkers, as skin biopsy is an easy and inexpensive technique," comments Donadio. "This approach could be particularly relevant when a specific treatment for synucleinopathies becomes available."

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ORIGINAL ARTICLES Donadio, V. *et al.* A new potential biomarker for dementia with Lewy bodies: skin nerve α-synuclein deposits. *Neurology* http://dx.doi.org/10.1212/WNL.0000000000004146 (2017)
FURTHER READING Elahi, F. M. & Miller, B. L. A clinicopathological approach to the diagnosis of dementia. *Nat. Rev. Neurol.* http://dx.doi.org/10.1038/nrneurol.2017.96 (2017)