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Exploring the presence of frontotemporal lobar degeneration associated proteinopathies in the skin: the skin as a possible biomarker for FTD?

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State of the art
Frontotemporal dementia (FTD) is heterogeneous with respect to its clinical presentation and underlying neuropathology, termed frontotemporal lobar degeneration (FTLD). Where three main subtypes are characterized by accumulation of either TDP-43, tau or FUS. Reliable ante-mortem biomarkers to identify FTD or its pathological subtypes are currently lacking. The skin provides the potential for a minimally invasive, accessible biomarker. The aim of this study is to assess the presence of the proteinopathies in the skin of FTLD donors.
Methodology
Post-mortem skin biopsies were obtained from the scalp of 7 FTLD donors of which one donor carried a *C9orf72* repeat expansion, and four non-FTLD donors. Biopsies underwent 24h-36h formalin fixation, followed by immunohistochemistry (IHC) for phosphorylated TDP-43 (pTDP-43), tau (AT-8), p62, dipeptide repeat proteins (DPRs) (poly-GA, poly-GR, poly-GP) and phosphorylation independent TDP-43 (panTDP-43). The presence of panTDP-43 in different skin structures was quantified based on area coverage using ImageJ software.
Results
We found no pTDP-43 or tau inclusions in the skin and expression of panTDP-43 was not increased in the epidermis, sweat glands and hair follicles. In the *C9orf72* repeat expansion carrier DPRs were identified throughout the epidermis and dermis with poly-GA presented most prominently.
Conclusion
These findings suggest to further explore the skin as a potential ante-mortem biomarker for FTLD and its subtypes with different antibodies, and to investigate whether DPR pathology in the skin could monitor disease progression in *C9orf72* carriers.

Conflicts of interest

N/A