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Reproducibility of FTLD-TDP subtypes among experienced diagnosticians

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State of the art: FTLD-TDP has been subdivided into 3 major subtypes (Types A-C), but many neuropathologists lack confidence in subtype classification or doubt the reproducibility of prevailing criteria. We sought to assess agreement among experts in diagnosing the 3 major FTLD-TDP subtypes.

Methodology: Three experienced raters selected 13 cases each from their home institutions: 9 “straightforward” (Types A-C, 3 each) and 4 deemed difficult to classify. Each rater presented cases via video conferencing-based live slide sharing to the other two raters, who were blinded to clinical, genetic, and pathological data. Raters rendered their classifications independently and were allowed to provide initial designations such as “unclassifiable” or “other” (e.g. “A + B”). When this occurred, raters were next required to engage in “forced choice”, designating each case as A, B, or C.

Results: Raters offered a Type A-C diagnosis in 24/27 straightforward cases, and agreement was substantial (overall Fleis kappa = 0.82; Type A = 0.83, B = 0.83, C = 0.94). Inclusion of challenging cases diminished agreement (overall Fleis kappa = 0.64). Forced choice improved agreement to nearly the level achieved for non-challenging cases (Fleis kappa = 0.79). These levels of agreement were achieved despite notable differences in approach across raters.

Conclusions: Reproducible FTLD-TDP subtype diagnosis is feasible among experienced diagnosticians, especially for straightforward cases. Although forced choice improves reproducibility, it may compromise validity. The next steps for this work are to revise neuropathologic criteria for Types A-C and test reproducibility among a larger group of raters.

Conflicts of interest

none