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Saturday

Phenoconversion observed over longitudinal follow-up in mutation carriers of familial Frontotemporal Lobar Degeneration in the ALLFTD Consortium,

Hilary Heuer, Danielle Brushaber, Adam Staffaroni, Toji Miyagawa, Leah Forsberg, Annie Clark, Edward Huey, Bradley Boeve, Adam Boxer, Howie Rosen, on behalf of the ALLFTD Consortium .

State of the Art
In familial FTLD, prediction of near-future clinical status may provide insights into opportunities for intervention. As therapeutic agents may have adverse effects or limited action, identifying disease onset through transitions from asymptomatic to prodromal disease, or from prodromal to overt disease, may reveal appropriate windows for disease-modifying treatments.

Methodology
The ALLFTD study identified familial FTLD (f-FTLD) participants carrying disease-associated mutations in *C9orf72*, *MAPT*, or *GRN* genes with at least two clinical assessment timepoints (range: 2-7; median 3) to determine disease transition points (phenoconversion). Clinical status was defined by the CDR+NACC-FTLD global score: "asymptomatic"=0, "prodromal/mild"=0.5, or "overt"=1+; phenoconversion was determined by transition from asymptomatic to prodromal (partial), asymptomatic to overt (definite), or prodromal to overt.

Results
262 participants (128 *C9*, 58 *GRN*, 76 *MAPT*) were evaluated for phenoconversion; 68 were excluded due to overt disease at the first visit. *MAPT* mutation carriers most often showed definite progression (7/43) from asymptomatic to overt over multiple visits. All definite converters (n=10) passed through "prodromal" (CDR+NACC-FTLD=0.5) at one or more intermediate visits, suggesting the prodromal stage may be variable in duration but indicative of impending full conversion. Moreover, partial conversions (CDR+NACC-FTLD 0 to 0.5) occurred in all cohorts (*GRN:* 6; *MAPT*: 6; *C9orf72*: 7), as did conversion from prodromal to overt (*GRN:* 5; *MAPT*: 9; *C9orf72*: 6).

Conclusions
Longitudinal assessment of clinical status in f-FTLD suggests the prodromal disease stage, captured by the CDR+NACC-FTLD, may provide a critical access window for disease-modifying treatment to avoid full phenoconversion to overt disease.

Conflicts of interest

Nothing to disclose.