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Sex influences clinical phenotype in frontotemporal dementia

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State of the art: Frontotemporal dementia (FTD) encompasses a wide spectrum of genetic, clinical, and histological findings. Sex is emerging as a potential biological variable influencing FTD heterogeneity; however, only a few studies explored this issue with nonconclusive results.
Methodology: Five hundred and thirty-one FTD patients were consecutively enrolled. Demographic, clinical, and neuropsychological features, survival rate and serum neurofilament light (NfL) concentration were determined and compared between sex.
Results: Behavioral variant of FTD was more common in men, whereas primary progressive aphasia was overrepresented in women ($p<0.001$). While global cognitive impairment was comparable, females had a more severe cognitive impairment, namely in Trail Making Test parts A and B ($p=0.003$), semantic fluency ($p=0.03$), Short Story Recall Test ($p=0.003$) and the copy of Rey Complex Figure ($p=0.005$). On the other hand, men exhibited more personality/behavioral symptoms (Frontal Behavior Inventory [FBI] AB, $p=0.003$), displaying higher scores in positive FBI subscales (FBI B, $p<0.001$). In particular, apathy ($p=0.02$), irritability ($p=0.006$), poor judgment ($p=0.033$), aggressivity ($p=0.008$), and hypersexuality ($p=0.006$) were more common in men, after correction for disease severity. NfL concentration and survival were not statistically different between men and women ($p=0.167$ and $p=0.645$, respectively).
Conclusion: The present study demonstrated that sex is a potential factor in determining FTD phenotype, whereas it does not influence survival. Although the pathophysiological contribute of sex in neurodegeneration is not well characterized yet, our findings highlight its role as deserving biological variable in FTD.

Conflicts of interest

N/A