In Response to a Letter to the Editor
“Frontotemporal Dementia and Suicide; Could Genetics be a Key Factor?”

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We thank Dr Fremont et al for their interest in our findings1 and for calling attention to some aspects that may need further explanation.

There is a need for a specific and standardized approach to the measurement of suicidal behaviors in patients with neurodegenerative disorders, in which neuropsychiatric symptoms often represent common clinical features.2 Furthermore, patients with behavioral variant frontotemporal dementia (bvFTD) are characterized since from early stages of the disease, more frequently in comparison to other forms of dementia, by a high level of anxiety, depression, apathy, and disinhibition.3 Previous studies reported that the presence of mood disorders and impulsivity is straight related to suicidal behavior.4 For this reason, it is important to perform an evaluation of risk of suicidality in bvFTD patients, also in the prodromal phase of the disease.

We agree with Dr Fremont et al that genetics background could contribute to suicide ideation, as well as behavioral, environmental, and neurobiological factors. In the last 20 years, different causative and susceptibility genes for FTD have been discovered. The 3 most common FTD genes are microtubule-associated protein tau (MAPT), progranulin (GRN), and chromosome 9 open reading frame 72 (C9orf72). In literature, patients carrying C9orf72 expansions showed an increased risk of suicide and other psychiatric features as late-onset psychosis.5,6 In our data set of patients with bvFTD, only one patient showed a missense mutation in GRN gene, and another one carried an expansion in C9orf72 gene. As we described in our study, due to the paucity of patients carrying mutations, we did not detect any clear link between suicide risk and mutations in known FTD-related genes. Thence, further studies are warranted to better evaluate whether differences in FTD genetic background can lead to different psychiatric symptoms.

Dr Fremont and colleagues assessed the risk of suicide in a FTD population with a clinical dementia rating (CDR) scores of 1 or less, while our bvFTD patients had a longer duration of the disease, and showed a mild or moderate dementia with a CDR mean of 1.5 ± 0.6. In addition, he did not find elevated suicidal ideation in bvFTD patients with a MAPT gene mutation and early or prodromal symptoms of the disease, while our results show that bvFTD population are at higher risk of suicide.

Intriguingly, both of studies are in contrast with most prior evidence on major risk factors related to suicidal behavior in dementias in which suicidality appears to be inversely associated with severity of disease.7 Therefore, it could be hypothesized that risk of suicide in the bvFTD patients can be influenced by other neuropsychological aspects, usually not assessed by Mini-Mental State Examination or CDR, such as behavioral changes, social cognition impairment, and psychiatric conditions. In line with this suggestion, in our bvFTD population,1 main risk factors for suicide include high levels of depression, anxiety, stress, and hopelessness.

For this reason, a wide and deep neuropsychiatric assessment, associated to the most common cognitive evaluation, can...

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represent a better clinical approach for these patients. Furthermore, it could be interesting, as already partly proposed by Dr Fremont, to understand whether there are environmental, neurobiological, or genetics factors that could affect the clinical features of the disease and particularly the severity of neuropsychiatric disorders. Additional studies with larger populations of FTD patients carrying mutations in the 3 major genes could allow to examine whether the differences in the genetics of FTD could influence psychiatric symptoms and also the risk of suicide.

These studies could provide additional information of the neurobiological mechanisms underlying frontotemporal dementia and open the avenue to personalized treatment.

Declaration of Conflicting Interests
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