

Neural functional changes in premanifest C9orf72-repeat expansion carriers

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State of the art: Behavioral variant frontotemporal dementia (bvFTD), the most common variant of FTD, is primarily characterized by changes in socio-emotional functioning. The most common genetic cause of FTD is an expansion of a GGGGCC repeat in the C9orf72 gene. The functional neural changes related to social cognition in premanifest C9orf72-repeat expansion carriers (C9-RE) remain elusive.

Methodology: We addressed this issue in 21 C9-RE and 24 neurotypical controls, by combining structural MRI, mass univariate and multi-voxel pattern analysis (MVPA) on task-based functional MRI data, relating to perception of houses and neutral and emotional faces, in addition to off-line behavioral assessments.

Results: The C9-RE group showed significantly decreased activation for social perception (faces vs houses) in the left inferior occipital area and a trend of decrease in the right anterior insula. Support vector machine analysis revealed above chance group classification in these areas. Representational similarity analysis also revealed significant higher similarity patterns in the left inferior occipital area in controls. The activation in the right insula and amygdala correlated negatively with the volume of the main atrophic area: the thalamus, in the C9-RE group. Furthermore, activation in the right insula and amygdala correlated positively with emotion recognition performance in the C9-RE group.

Conclusion: These findings reveal converging support for the functional changes and effects at distance of structural changes in premanifest C9-RE, related to social cognition. Task-based functional imaging may have high potential as biomarker of social impairment in premanifest FTD and neurodegeneration in general.

Conflicts of interest

The authors report no competing interests.