LETTER TO THE EDITOR

Considering the frontomedian cortex in revised criteria for behavioural variant frontotemporal dementia

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Sir, Recently, an international consortium developed revised guidelines for the diagnosis of behavioural variant frontotemporal dementia (FTD) based on histopathologically confirmed cases and their clinical symptoms (Rascovsky et al., 2011). The revised criteria suggest that ‘possible’ behavioural variant FTD requires three of six clinically discriminating features (disinhibition, apathy/inertia, loss of sympathy/empathy, perseverative/compulsive behaviours, hyperorality and dysexecutive neuropsychological profile). ‘Probable’ behavioural variant FTD adds functional disability and characteristic neuroimaging (frontal and/or anterior temporal atrophy, hypometabolism or hypoperfusion), while behavioural variant FTD ‘with definite frontotemporal lobar degeneration’ requires histopathological confirmation or a pathogenic mutation. The study revealed a much higher sensitivity of the proposed criteria in comparison to earlier criteria (Neary et al., 1998) in a multi-site sample of 137 patients with pathologically verified frontotemporal lobar degeneration. These results will obviously greatly advance the early identification of behavioural variant FTD, which is particularly relevant for early treatment.

Recent comprehensive systematic and quantitative meta-analytic neuroimaging approaches with the anatomical likelihood estimate method conducted according to quality standards of the QUOROM statement enabled the identification of the prototypical neural networks involved in neurodegenerative diseases such as behavioural variant FTD (Schroeter et al., 2007, 2008, 2009). These studies including 132 patients with behavioural variant FTD, together with other multi-centre imaging approaches (Salmon et al., 2003) and histopathological studies focusing on von Economo neurons (Seeley et al., 2006) suggest that behavioural variant FTD is related to atrophy and hypometabolism mainly in frontomedian brain regions, the anterior insula and the thalamus. Beside frontal areas, no temporal clusters were identified, indicating that behavioural variant FTD is mainly a frontomedian disease. Anterior temporal atrophy was, in contrast, observed in Alzheimer’s disease and semantic dementia in these anatomical likelihood estimate meta-analyses—decreasing the discriminating specificity of this brain region (Schroeter and Neumann, 2011).

The affected frontomedian clusters in behavioural variant FTD have been associated with social cognition, in particular, theory of mind abilities (Amadio and Frith, 2006), which are known to be specifically impaired in this disease (Gregory et al., 2002; Adenzato et al., 2010). Surprisingly, the new criteria do not include neuropsychological testing of social cognition—a fact that might be related to the traditional neglect of the functions of the frontomedian cortex in test batteries in contrast to the well-known sensitivity of executive tests mainly for the frontolateral cortex (Schroeter et al., 2012). One might argue that the new diagnostic criteria already include empathy. However, empathy is a concept different from theory of mind—whereas empathy represents a sharing of another’s state, theory of mind affords only an understanding of this state. Furthermore, neural networks involved in empathy do not cover the anterior frontomedian cortex (Rankin et al., 2006; Hein and Singer, 2008; Fan et al., 2011), which is the core region affected by behavioural variant FTD (Salmon et al., 2003; Schroeter et al., 2007, 2008).

In conclusion, adapting diagnostic criteria by specifying imaging criteria and adding neuropsychological data with an emphasis on social cognition (in particular, theory of mind) might further increase the revised criteria’s specificity, reliability and predictive power in the early stages of behavioural variant FTD, when
disease-modifying interventions are likely to be most effective (Rascovsky et al., 2011).

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**References**


