Neuroanatomical correlates of social cognition in behavioral-variant frontotemporal dementia using the Social Norms Questionnaire

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Introduction

Behavioral variant frontotemporal dementia (bvFTD) is a neurodegenerative disorder that is often misdiagnosed as Alzheimer's disease (AD). Patients with bvFTD present with marked deficits in social cognition and adherence to social conventions. Few measures exist to reliably differentiate between bvFTD and AD, as the diagnosis of bvFTD relies primarily upon historical information provided by caregiver informants. The Social Norms Questionnaire (SNQ) is a neuropsychological measure that can be used to aid in the differential diagnosis of bvFTD from AD.

Objective

To validate the Social Norms Questionnaire as a screening measure to be used for diagnostic purposes, as well as to identify neuroanatomical correlates of social cognition.

Methods

Twenty-six participants were included in the study, 11 patients diagnosed with bvFTD (Age, *M* = 59.6 years, SD = 10.95) and 15 with AD (Age, *M* = 59.5, SD = 5.97) were recruited from the Frontotemporal Dementia and Neurobehavior Clinic at UCLA. The two groups did not differ significantly on any demographic characteristics (Table 1). The Mini-Mental State Examination (MMSE) was administered to screen for cognitive impairment. None of the subjects had severe cognitive impairment.

Table 1: Demographic Information

	bvFTD (N=11)	AD (N=15)	*p*
Age, y	59.6 (10.9)	59.5 (5.9)	n.s.
Age of Onset, y	55.5 (10.2)	55.6 (7.2)	n.s.
Edu, y	15.3 (2.0)	16.5 (1.95)	n.s.
MMSE, total	23.6 (4.8)	24.6 (4.3)	n.s.
Gender	5M/6F	5M/10F	*n.s.

*Note: * Chi-square*

All twenty-six participants were given the Social Norms Questionnaire (SNQ). The SNQ contains 22 items/statements pertaining to social behaviors. Participants respond either 'yes' or 'no' regarding whether a specific behavior is considered socially appropriate in mainstream US culture. A total score is obtained by summing correct items (22 possible). Two subscales are calculated, Overadhere errors and Break errors. Break errors refer to endorsement of a socially inappropriate behavior (i.e. eating pasta with your fingers) as appropriate. Overadhere errors refer to endorsement of a socially appropriate behavior (i.e. eating ribs with your fingers) as inappropriate.

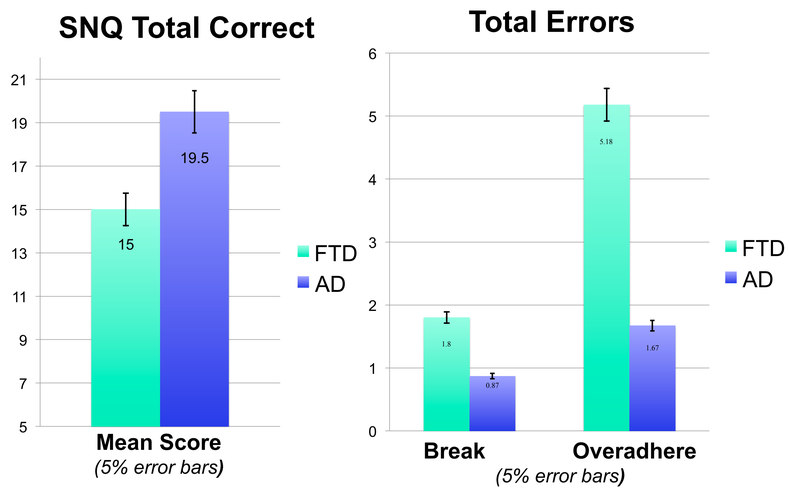
MRI Protocol

All subjects were scanned in the same 1.5T MRI scanner. High-resolution T1-weighted 3D MRI scans were acquired in the coronal plane using a 3-D MP-RAGE sequence. An automated Brain Surface Algorithm (BSE) was applied, with manual editing to generate a deskulled brain volume. To adjust for differences in brain positioning and scale across individuals, scans were linearly registered to the stereotaxic space (per International Consortium for Brain Mapping (ICBM)[1]). Aligned images had a final voxel size of 1 mm^3.

Results

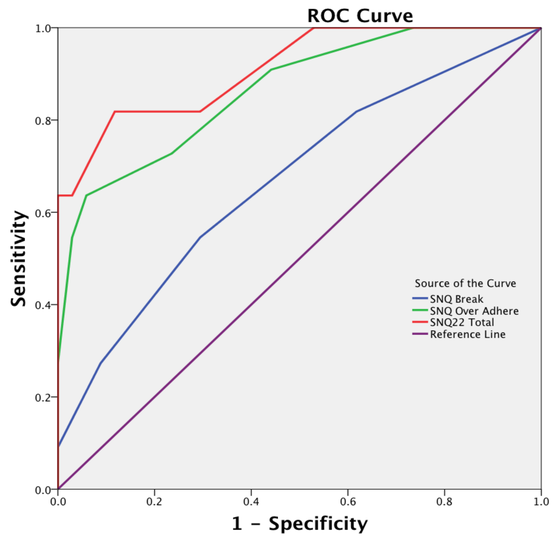
An individual change map, or Jacobian map, was computed by non-linearly registering each scan to a template brain. For each subject, a local tissue difference map was obtained by calculating the local Jacobian determinant relative to the normal template. Values of ±0.1 would indicate that specific volumetric regions were respectively smaller or larger relative to the normal template by 10%. All results and statistical analyses are based on the Jacobian maps.

Figure 1: SNQ Total; Overadhere and Break errors



Significant group differences were found on SNQ total score t(24) = -5.31, p<.001 and Overadhere score score t(24) = 3.72, p=.002

Figure 2: Receiver Operating Curve Demonstrating diagnostic utility of the SNQ



SNQ total score <18 points, Area Under the Curve (AUC) = .912, p<.001, sensitivity/specificity 82%/88%. Overadhere score >2 errors, AUC =.864, p<.001, 73%/76%. Break AUC=.668, p=.10.

After controlling for age and diagnosis in a partial correlation, in a portion of the total sample (with both SNQ and neuroimaging; n=20, bvFTD=9; AD=11), a higher Break score was correlated with lower volume in the anterior temporal lobe (*r* = -.469, *p* =. 049) greater in the right hemisphere (*r* = -.51, *p* = .031) than the left (*r* = -.296, *p* =.234). A trend was observed between Break score and right orbitofrontal volume (*r* = -.399, *p* = .10). There were no significant correlations between either SNQ total or Overadhere score and brain volume in any regions of interest.

Figure 3: Scatterplot displays association between Anterior temporal volume and SNQ break score

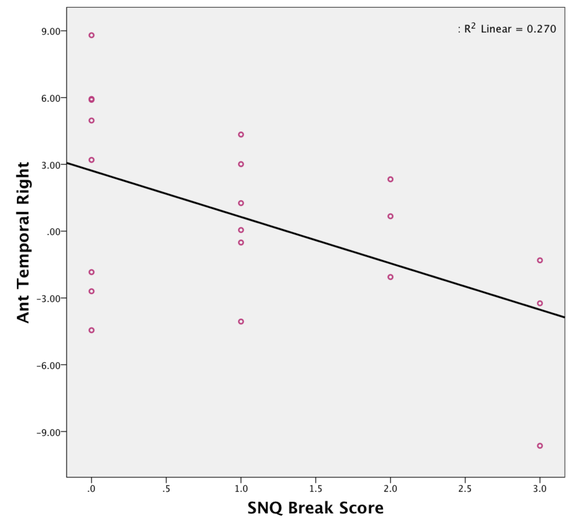
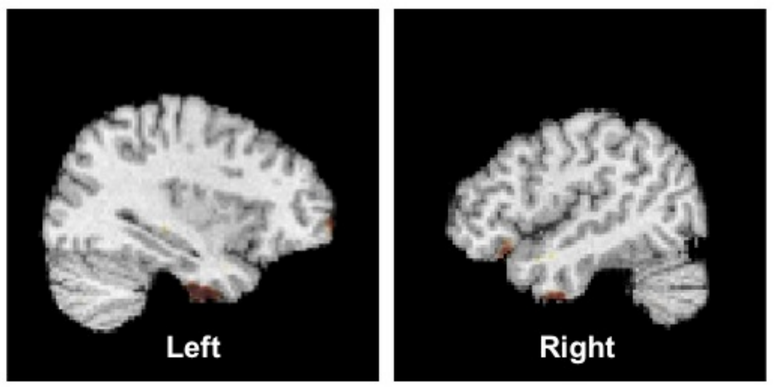


Figure 4: Images of TBM maps and SNQ Break Score correlates with bilateral anterior temporal lobe volume



Discussion

The results of this study suggest the Social Norms Questionnaire is a quick and accurate screening measure which distinguishes bvFTD from AD. Patients with bvFTD had lower SNQ scores, suggesting that they have deficits in recognizing social norms compared to those with AD. Greater 'Overadhere' errors in the bvFTD group may be due to concrete cognitive errors and failure to appreciate the emotional responses of others. SNQ Total Score and Overadhere score accurately discriminates bvFTD and AD, displaying the clinical utility of the measure. Additionally, greater endorsement of social norm violations (break errors) in the total sample was associated with reduced volume in the anterior temporal lobe, particularly in the right hemisphere, which is implicated in maintenance of appropriate social behavior, personality change, and nonverbal semantic knowledge.

Acknowledgements

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