Oops! Resolving social dilemmas in frontotemporal dementia

Paul J Eslinger, Peachie Moore, Vanessa Troiani, Shweta Antani, Katy Cross, Shaleigh Kwok, Murray Grossman

Objectives: Our social cognition model posits that social knowledge and executive resources guide interpersonal decision making. We investigated this model by examining the resolution of standardised social dilemmas in patients with a social and executive disorder (SOC/EXEC) caused by frontotemporal dementia (FTD).

Methods: Patients with SOC/EXEC (n = 12) and those with progressive aphasia (APH, n = 14) completed measures requiring resolution of social dilemmas (Guilford’s Cartoon Predictions Test), social cognition (theory of mind false belief vignettes and a behavioural rating measure of empathy) and executive measures of cognitive flexibility (Visual Verbal Test). Regression analysis related judgments of social dilemmas to cortical volume using voxel based morphometry of high resolution structural MRI.

Results: Patients with SOC/EXEC were impaired in judgments of social dilemmas as well as theory of mind, self-awareness of empathy and cognitive flexibility. Patients with APH were much less impaired in the social and cognitive measures. There were strong correlations among social dilemma, theory of mind and mental flexibility measures in patients with SOC/EXEC, and stepwise regression showed that mental flexibility was most predictive of social dilemma judgments. Social dilemma impairments in the SOC/EXEC sample correlated with cortical atrophy in the orbital frontal, superior temporal, visual association and posterior cingulate regions of the right hemisphere.

Conclusions: Deficits in patients with SOC/EXEC in resolving social dilemmas are related to depleted executive resources and social knowledge that appear to arise from disease that interrupts a right frontal–temporal neural network crucial for mediating social cognition.
choice and a suboptimal choice). Performance was not timed. A practice item established that participants understood the task.

Theory of mind
Twelve vignettes assessed facts and beliefs about characters in social situations.21 Each scenario was presented with lie and joke conditions that required contrasting decisions about a main character’s first order beliefs, and the second order beliefs that another character held of the main character. In the lie condition, the story’s agent was not aware that they were observed in the offending act; in the joke condition, the agent was aware that they were observed by the confronting character. Second order belief questions required interpretation of whether the character was lying to avoid getting caught or joking to cover up embarrassment. Vignettes were read aloud and concurrently presented in writing. A practice vignette established that participants understood the task.

Visual verbal test
This non-social measure of executive resources required abstraction and cognitive flexibility. Stimulus sets were four geometric designs on a single page.22,23 Three designs were categorised in two different ways based on similarity in colour, shape, size or orientation. Participants identified how three designs were alike, then how three designs were alike in another way (eg, three designs black, three designs triangular). First choice accuracy ranged from 0 to 10. Second choice accuracy was computed relative to the first choice score (range 0–100%). Ten stimulus sets were presented. A practice item ensured comprehension.

Empathy ratings
Patients/caregivers and controls/spouses each completed three questions assessing empathic behaviours in daily social settings.24 Discrepancies were computed to measure metacognitive awareness. Ratings varied from 0 to 100, with higher scores representing more adept empathic behaviour.

Imaging procedure
In patients with SOC/EXEC, high resolution structural MRI images were obtained using a Siemens 3.0-T MRI scanner. After rapid sagittal T1 weighted imaging to determine patient position, high resolution T1 weighted 3D MPRAGE images were acquired with a repetition time of 1620 ms, echo time of 30 ms, 1 mm slice thickness, flip angle of 15°, matrix size of 192×256 and rectangular field of view giving an in-plane resolution of 1.0×1.0 mm. Brain volumes were registered in SPM9941 using 12 parameter affine registration, non-linear registration using 12 non-linear iterations and 7×8×7 basis functions. Brains were normalised to the T1 template of 305 averaged brain volumes with standardised brain coordinates using a high dimensional normalisation procedure.44 Brain volumes were segmented into four tissue types (gray matter, white matter, CSF and other). The segmentation algorithm in SPM99 calculates a Bayesian probability for each tissue type voxel in the volume, based on a priori MRI information. We inspected each slice of each segmented volume to ensure that no voxels from the dural sinuses or adjacent non-brain structures were misclassified as gray matter. Using SPM99, the gray matter volume was smoothed with a 12 mm FWHM Gaussian filter to minimise individual gyral variations.

Voxel based morphometry in SPM99 analysed brain volumes.46 A proportional analysis threshold included only voxels with 40% or more of the grand mean value. Implicit masking was used to ignore zeros, and global calculation was based on the mean voxel value. SPM99 analyses included a two sample t test routine to compare the gray matter volume of patients with SOC/EXEC with 12 healthy age matched controls. Statistical threshold for atrophy studies relative to controls was set at p<0.0001. We did not correct for multiple comparisons because of the hypothesis driven nature of the analyses. Moreover, the small size of the voxels would make Bonferroni-like statistical correction too conservative. Instead, clusters of 100 or more adjacent voxels were considered, reflecting a statistically robust effect exceeding p<0.05 corrected for multiple comparisons in this neuroanatomical distribution.45 Regression analysis relating cartoon prediction score to gray matter atrophy, derived from contrast of cortical volume, was compared in the SOC/EXEC and control groups. Statistical threshold for this analysis was set at p<0.001 uncorrected, requiring >100 adjacent voxels/clusters.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>SOC/EXEC</th>
<th>APH</th>
<th>Total FTD</th>
<th>Control</th>
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<tbody>
<tr>
<td>n</td>
<td>12</td>
<td>14</td>
<td>26</td>
<td>17</td>
</tr>
<tr>
<td>Age (y)</td>
<td>66.17</td>
<td>71.92</td>
<td>69.16</td>
<td>75.07</td>
</tr>
<tr>
<td>Education (y)</td>
<td>14.83</td>
<td>14.73</td>
<td>14.78</td>
<td>15.14</td>
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<tr>
<td>MMSE (max = 30)</td>
<td>22.38</td>
<td>23.45</td>
<td>23.00</td>
<td>29.33</td>
</tr>
<tr>
<td>Cartoon predictions (%)</td>
<td>44.17 (27.12)</td>
<td>61.54 (21.54)</td>
<td>53.20 (25.45)</td>
<td>84.71 (17.36)</td>
</tr>
<tr>
<td>Visual Verbal Test (%)</td>
<td>First Choice 89.17 (19.75)</td>
<td>100 (0.00)</td>
<td>94.80 (24.47)</td>
<td>100 (0.00)</td>
</tr>
<tr>
<td></td>
<td>Second Choice 48.56 (28.17)</td>
<td>74.62 (31.52)</td>
<td>62.11 (32.18)</td>
<td>92.67 (8.84)</td>
</tr>
<tr>
<td>Theory of mind (%)</td>
<td>First question 96.30 (6.05)</td>
<td>98.15 (3.67)</td>
<td>97.22 (4.95)</td>
<td>100 (0.00)</td>
</tr>
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<td></td>
<td>First order belief 86.11 (14.43)</td>
<td>89.81 (9.11)</td>
<td>87.96 (11.86)</td>
<td>98.62 (3.40)</td>
</tr>
<tr>
<td></td>
<td>Second-order belief 56.48 (21.96)</td>
<td>60.19 (13.68)</td>
<td>58.33 (17.84)</td>
<td>83.33 (14.91)</td>
</tr>
<tr>
<td></td>
<td>Second-order interpretation 44.44 (11.02)</td>
<td>60.19 (19.89)</td>
<td>52.31 (17.57)</td>
<td>80.56 (14.59)</td>
</tr>
<tr>
<td>Empathy rating (%)</td>
<td>Self rating 81.67 (21.01)</td>
<td>75.33 (12.59)</td>
<td>78.15 (16.62)</td>
<td>84.44 (16.67)</td>
</tr>
<tr>
<td></td>
<td>Caregiver rating 39.17 (14.44)</td>
<td>69.33 (18.91)</td>
<td>55.93 (22.65)</td>
<td>85.92 (13.10)</td>
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<tr>
<td></td>
<td>Self/caregiver discrepancy 42.50 (24.15)</td>
<td>6.00 (12.35)</td>
<td>22.22 (25.87)</td>
<td>1.46 (17.25)</td>
</tr>
</tbody>
</table>

| Characteristics and test scores for patients with frontotemporal dementia and controls |   |

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Impaired social judgments in patients with frontotemporal dementia with a SOC/EXEC disorder were associated with ToM and cognitive flexibility deficits, and related to right hemisphere cortical atrophy in the orbital frontal, superior temporal, visual association and posterior cingulate regions. These findings support a social cognition model encompassing interacting social knowledge and executive resources in a large scale neural network involving the right frontal and temporal regions. Deficits in APH were less severe and infrequent, although further investigation of APH social disorders are needed.

Cartoon predictions monitor crucial aspects of social behaviour that are compromised in SOC/EXEC. Successful performance requires perception of characters and their mental states within specific social situations, and resolution of the social predicament by choice of subsequent actions. Patients with SOC/EXEC were profoundly impaired in social judgment and deficient in cognitive flexibility, an executive resource that was highly predictive of impaired social judgments. ToM was also highly correlated with social judgment. Together with reduced empathy, these findings suggest important inter-relationships of social and cognitive domains in a social executor framework in FTD patients with SOC/EXEC. Impaired social judgment in SOC/EXEC was associated with right hemisphere cortical atrophy in the orbital frontal, superior temporal gyrus/sulcus, extrastriate and posterior cingulate regions that have been linked to social and emotional impairments and to social–moral emotion, empathy, sympathy and a mentalising circuit.

We hypothesise that social executors encompass knowledge and executive resources. Social knowledge elaborates the store of emotional responses to current social predicaments. Social knowledge of past social predicaments is stored in the posterior cingulate regions. Toward an understanding of how social executors interact with social knowledge, social–moral empathy, sympathy and a mentalising circuit. This interaction is supported by the social knowledge model.
of social actions, experiences and sequences that are bound by learned rules, conventions and conditional probabilities. Effective implementation of this knowledge is constrained by processing resources that are specific to the social domain (e.g., ToM, empathy sensitivity) and domain–neutral executive resources (e.g., cognitive flexibility). Patients with SOC/EXEC suffer progressive losses in both social knowledge and associated processing resources that cause social disability. This is related to pathology in a neural network encompassing the right orbital frontal and superior temporal regions.

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REFERENCES