Case Report/Case Series

Comparing Moral Judgments of Patients With Frontotemporal Dementia and Frontal Stroke

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IMPORTANCE Several clinical reports have stated that patients with prefrontal lesions or patients with the behavioral variant of frontotemporal dementia share social cognition impairments. Moral reasoning is impaired in both conditions but there have been few investigations that directly compare this domain in the 2 groups. This work compared the moral judgments of these patient groups using a task designed to disentangle the contributions of intentions and outcomes in moral judgment.

OBSERVATIONS For both disorders, patients judged scenarios where the protagonists believed that they would cause harm but did not as being more permissible than the control group. Moreover, patients with frontotemporal dementia judged harmful outcomes in the absence of harmful intentions as less permissible than the control participants. There were no differences between the 2 conditions.

CONCLUSIONS AND RELEVANCE Both disorders involved impairments in integrating intention and outcome information for moral judgment. This study was the first, to our knowledge, to directly compare a social cognition domain in 2 frontal pathologies with different etiology. Our results highlighted the importance of comparing patients with vascular lesions and patients with neurodegenerative diseases.

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More than a century ago, the Phineas Gage case revealed that frontal lobe lesions can cause personality and social cognition impairment. Since its description, clinical observations[1] have highlighted important similarities between the symptoms of patients with prefrontal lesions (PFL) and patients with the behavioral variant of frontotemporal dementia (bvFTD). Both conditions share symptoms such as distractibility, personality changes, social inappropriateness, and markedly impaired moral judgments.[2,3] However, to our knowledge, no studies have compared PFL and bvFTD regarding any social cognition domain.

Social cognition tasks are particularly sensitive in detecting impairment in frontal patients.[4] Moral reasoning is a social cognition domain affected in both conditions.[2,3] The brain areas usually affected in bvFTD[5,6] (the ventromedial prefrontal cortex [VMPC], orbitofrontal cortex, anterior temporal lobes, amygdala, and insula) are involved in moral cognition.[7] Moreover, patients with VMPC damage show abnormal moral judgments of harmful intentions in the absence of harmful outcomes.[3] However, to our knowledge, no studies of bvFTD have previously examined the processing of intentions and outcomes in moral judgment.

This work compared the moral judgments of patients with bvFTD and patients with PFL by means of a well-characterized task[3] involving scenarios that disentangle the contributions of intentions and outcomes to moral judgment.

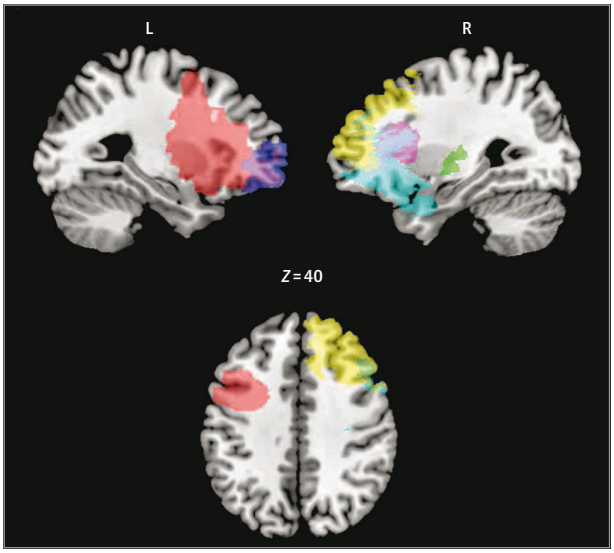
Methods

Participants

All participants provided written informed consent in agreement with the Helsinki declaration. The ethics committee of the Institute of Cognitive Neurology approved this study. Eight patients with unilateral chronic cerebrovascular lesions confined to frontal structures (**Figure 1**) were recruited. All patients were assessed at least 6 months after the lesion and none of them had aphasia or motor difficulties.

Nineteen patients fulfilled the revised criteria for probable bvFTD.[8] All patients underwent neurological, neuropsychiatric, and neuropsychological examinations and were in the early or mild stages of the disease. Patients with bvFTD and patients with PFL with psychiatric disorders, other neurological diseases, or diffuse brain damage in neuroimaging were excluded.

Figure 1. Lesions of Patients With Prefrontal Lesions



Left and right medial (top) and axial section (bottom) views. Each lesion is shown with a different color. L indicates left and R, right.

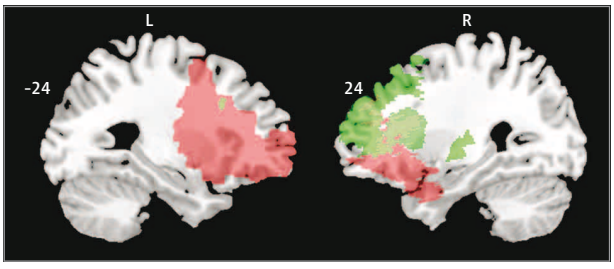
The performances of patients with PFL and patients with bvFTD were compared with the performances of 8 and 19 healthy control participants, respectively (matched by relevant variables, eTable in the Supplement). Individuals with a history of psychiatric or neurological diseases were excluded.

Magnetic Resonance Imaging Assessment

All patients with PFL underwent magnetic resonance scans at least 6 months after the lesion. The lesions were mapped using MRIcro software. These maps were normalized to a standard template using the statistical parametric mapping-5 software with cost-function masking.[9] Each patient's lesions were mapped on a standard brain (Figure 1).

For each patient, we calculated the percentage of each region included in the lesion. For a subgroup analysis, the patients were divided into 2 subgroups based on whether the VMPC was involved or not. Thus, 37.5% of the patients were classified as having VMPC involvement(**Figure 2**).

Figure 2. Lesions of Patients With and Without Involvement of the Ventromedial Prefrontal Cortex (VMPC)



Left and right brain medial views of patient lesions with (red) and without (green) VMPC damage. L indicates left and R, right.

Moral Judgment Task

General cognitive state and premorbid IQ were assessed (eAppendix 1.2 in the Supplement). Following the protocol reported elsewhere,[3,10] we presented the participants with 24 scenarios. Four variations of each scenario followed a 2 × 2 design; the protagonists either harmed another person (negative outcome) or did no harm (neutral outcome) or the protagonists either believed that they would cause harm (negative intention) or believed that they would cause no harm (neutral intention). Each possible belief was true for 1 outcome and false for the other outcome. Thus, the 4 scenarios were as follows: (1) no harm, (2) accidental harm, (3) attempted harm, and (4) successfully attempted harm. After reading each story, the participants were asked to rate the scenario on a Likert scale ranging from totally permissible (7) to totally forbidden (1) (details in eAppendix 1.1.1 in the Supplement).

Data Analysis

Demographic and neuropsychological data were compared using analysis of variance (ANOVA) and χ^2 tests for the categorical variables. Moral judgments were analyzed using mixed ANOVA. The planned comparisons were performed using 1-way ANOVA corrected with Tukey Honestly Significant Difference tests. To compare the performance of patients with bvFTD and patients with PFL, we performed ANOVA-adjusted comparisons for the moral judgments of their respective control participants. Intragroup comparisons were also performed (eAppendix 1.2 in the Supplement). We used a nonparametric test to compare the performance of patients with PFL with and without VMPC involvement. Finally, we performed multiple single-case analyses using a modified 1-tailed t test.[11,12] This method allows the comparison of the score of each of the 3 patients with VMPC involvement with scores obtained by the group of 5 patients without VMPC lesions. This test is recommended for single-case analysis, is more robust for nonnormal distributions, and presents low values of type I error. The effect sizes (z_{cc}) were obtained using the same methods previously reported as point estimates.[13]

Results

Please see the eTable in the Supplement for the general cognitive status results (details in eAppendix 2.1 in the Supplement).

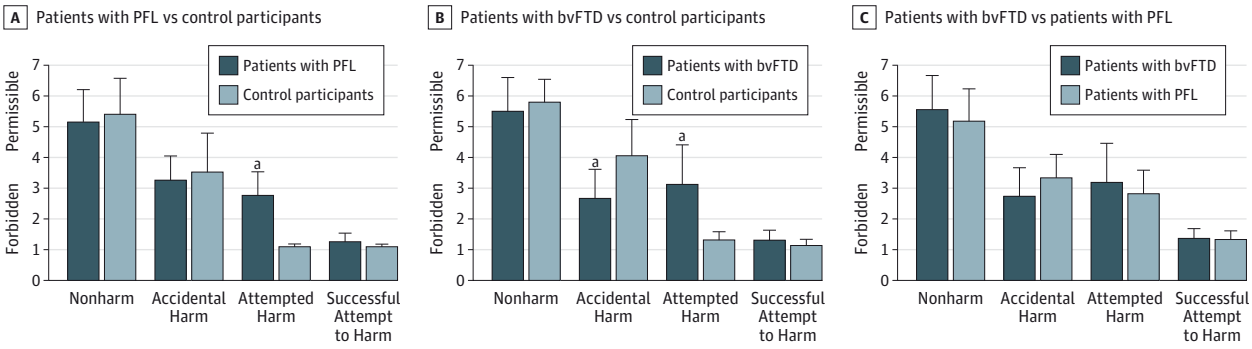
Moral Judgments

Figure 3 shows the moral judgments for each group.

Patients With PFL vs Control Participants

An interaction between intention and group ($F_{1,14}$ = 5.04, P < .05) and a tendency for outcome × group interaction ($F_{1,14}$ = 4.30, P = .06) were both identified. The planned comparisons revealed that patients with PFL judged attempted harm as more permissible than the control participants ($F_{1,14}$ = 32.14, P < .01). No significant differences were observed for the other scenarios (eResults 2.2.1 in the Supplement).

Figure 3. Moral Judgments and Significant Differences Between Groups



Patients with profrontal lesions (PFL) and patients with the behavioral variant of frontotemporal dementia (bvFTD) judged attempted harm as significantly more permissible than the control participants. Patients with bvFTD judged accidental harm as less permissible than did the control participants.

Patients With bvFTD vs Control Participants

Significant interactions were observed between intention and group ($F_{1,36}$ = 31.26, P < .01) and between outcome and group ($F_{1,36}$ = 27.19, P < .01). The planned comparisons showed that patients with bvFTD judged accidental harm as less permissible ($F_{1,36}$ = 27.19, P < .01) and attempted harm as more permissible than the control participants ($F_{1,36}$ = 30.05, P < .01). There were no significant differences for the other scenarios (eAppendix 2.2.2 in the Supplement).

Patients With PFL vs bvFTD

There were no significant differences in any of the conditions (see eAppendix 2.2.3 in the Supplement). The covariate with the control condition (paired cases) did not show a significant effect in any of the analyses.

Considering that the statistical significance depends, among other factors, on the variability of each group, we reanalyzed the data on the patients with PFL and bvFTD, excluding the participants who were below (minus 2 SDs) or above (plus 2 SDs) the group mean. The results showed that patients with bvFTD judged accidental harm as less permissible than the patients with PFL ($F_{1,22}$ = 5.98, P < .05) (see details in eAppendix 2.2.3 in the Supplement).

Intragroup Comparisons

Intragroup comparisons revealed that the patients with PFL and bvFTD were able to discriminate the content of the intentions and outcomes (details in eAppendix 2.2.4 in the Supplement).

No significant differences were detected in any condition between patients with and without VMPC involvement including nonharm (z = −0.44, P = .65), accidental harm (z = 0.74, P = .44), attempted harm (z = −0.14, P = .88), and successfully attempted harm (z = 0.89, P = .97). The results of the multiple single-cases analyses (eAppendix 2.2.4 in the Supplement) also showed that the performance of each patient with VMPC damage was similar to that of patients without VMPC involvement.

Discussion

Similar moral-cognition impairments have been reported in patients with PFL[14] and patients with bvFTD[2] but no previous research, to our knowledge, directly compared this domain between these 2 groups. The results of this study suggest that the moral judgment abnormalities in both groups are related to an impaired integration of intentions and outcomes.

Moral Judgment Abnormalities

A previous study[3] using the same scenarios showed that patients with bilateral VMPC damage judged attempted harm as more morally permissible than the control participants. We replicated these findings in a sample of patients with unilateral PFL not restricted to the VMPC. We found no differences between the moral judgments of patients with PFL with and without VMPC damage. Thus, our results suggest that not only bilateral VMPC lesions but also unilateral damage to other prefrontal regions can trigger this specific moral judgment impairment.

Moreover, regarding bvFTD, we found the same impairment in judging attempted harm. However, these patients also exhibited abnormal moral judgment of accidental harm. The patients with bvFTD were less willing than the control group to exonerate protagonists for accidentally causing harm. Exculpating an agent who causes harm accidentally requires an especially robust representation of the intentions, as it is necessary to use this information to override a preponderant negative response to the outcome.[15] Therefore, judgments of accidental harm particularly involve the capacity to integrate information about the agent's intention with contextual cues of the situation, a process that seems to be impaired in bvFTD.[5]

No differences between patients with bvFTD and PFL were observed in any of the scenarios. However, reanalysis of data excluding the outliers revealed that the patients with bvFTD judged accidental harm as less permissible than the patients with PFL. This result suggests that despite a common moral

cognition impairment in both conditions, subtle differences may be evident in larger samples.

Regarding the common patient group impairment and in contrast to neurotypical individuals,[15] patients with bvFTD and PFL judged attempted harm by focusing on the neutral outcomes instead of the protagonists' negative intentions. Thus, the performance of both groups is characterized by an overreliance on outcome rather than by the integration of intentions and outcomes.

In addition, patients with bvFTD judged accidental harm by considering the negative outcomes without the neutral intentions. A previous study assessed patients with high-functioning autism[16] on the same scenarios used here. Similar to patients with bvFTD, individuals with high-functioning autism exhibit real-life difficulties in social interaction but often succeed in laboratory tests. Furthermore, patients with high-functioning autism showed the same deficit in judging accidental harm observed in bvFTD. This pattern of results may reflect a moral-judgment impairment characterized by an underreliance on information about a person's innocent intentions and, as a direct result, an overreliance on the action's negative outcome.[16]

Implications for Theoretical Approaches

Neuroimaging[7] and lesion studies[3] suggest a specific role of certain areas in moral judgment, eg, the VMPC is crucial in evaluating harmful intent. In this study, patients with PFL (with and without VMPC damage) exhibited similar performance. Moreover, although VMPC may be affected in bvFTD, the atrophy pattern of these patients extends to other frontotemporal areas, including the orbital regions, amygdala, insula, right temporal pole, and white matter tracts.[6,17] The frontoinsular-temporal involvement should impact the bvFTD moral judgments.[18] Thus, our preliminary results indicate that impairment in patients with lesions that exclude the VMPC and patients with frontotemporal affectation may be comparable with the impairment in patients with focal VMPC lesions. Further studies should assess larger samples of patients with PFL with and without VMPC damage.

Both groups of patients showed similar behavioral impairment in moral cognition. Our findings suggest that moral judgment may be dependent on frontotemporal networks. Supporting this view, the event-feature emotion complex model[7] proposes that moral cognition is not restricted to VMPC but emerges from the integration of content and context-dependent representations in the cortical (frontal and temporal) and limbic networks. In line with this approach, the social context network model[5] describes the contextual influence on social cognition processing as dependent on a frontoinsular-temporal network that is consistently affected in bvFTD.[6] Moreover, frontotemporal connections can also be damaged by vascular PFL. Further neuroimaging and lesion studies should be performed to establish the specific neural regions and networks involved in the processing of intentions and outcomes in moral judgment.

Although our results are preliminary, they constitute the first direct comparison of the moral judgments of patients with 2 frontal pathologies of different etiology. These findings highlight the importance of studies comparing social and cognitive processes in patients with vascular lesions and patients with neurodegenerative diseases.[19]

ARTICLE INFORMATION

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Acquisition, analysis, or interpretation of data: Baez, Cuoto, Torralva, Sposato, Huepe, Montanes, Reyes, Matallana, Viglieca, Slachevsky, Ibanez.
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Statistical analysis: Baez, Cuoto, Huepe, Ibanez.
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