ORIGINAL ARTICLE

Analyzing theory of mind impairment in patients with behavioral variant frontotemporal dementia

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Abstract

Objective Behavioral variant frontotemporal dementia (bvFTD) and theory of mind (ToM) have common neuroanatomical aspects. This pilot study analyzed the qualitative features of ToM relatively to the site of prefrontal atrophy, aiming to identify a neurobehavioral pattern of bvFTD.

Method Fourteen bvFTD patients were compared with 14 healthy subjects with similar age, years of schooling, gender distribution, and social background. The faux pas task (FPT) measured the recognition and comprehension of faux pas (FP) and awareness of the factual details on 20 stories. Magnetic resonance assessed prefrontal atrophy.

Results The bvFTD patients were significantly impaired in FP recognition and comprehension and in attribution of non-existent FP. Qualitative analysis revealed five types of errors: misidentification of characters, misidentification of emotions, excessive cohesiveness to the factual context, delusional interpretations, and non-responses. The FPT recognition and comprehension scores were unrelated to story factual details or other neuropsychological performance. Conversely, the FP comprehension scores related to disease duration, the delusional errors to disease duration and prefrontal orbital atrophy, and the cohesiveness errors to age and prefrontal dorsolateral atrophy.

Conclusions In bvFTD, ToM is characterized by misinterpretation of mental states and concrete thinking, which is related to disease severity and distinct areas of prefrontal atrophy. This neurobehavioral pattern may be a marker for bvFDT.

Keywords Theory of mind · Social cognition · Executive functions · Orbital cortex · Cognitive impairment

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Introduction

Behavioral variant frontotemporal dementia (bvFTD) [1–3] usually presents with changes in empathy and social tact, self-centeredness, emotional blunting and disregulation, disinhibition, loss of insight, and stereotypic behavior, which are sooner or later followed by cognitive deficits [4]. These phenomena are attributed to degeneration in brain areas typically affected by bvFTD (e.g., the anterior medial and orbital prefrontal cortex, anterior cingulated gyrus, and basal ganglia) [5, 6]. However, other neurodegenerative disorders may affect the same brain regions and cause similar symptoms [4].

Most neuropsychological studies comparing bvFTD with Alzheimer's disease (AD) found no differences [7–15] or inconstant impairments in orofacial praxis [16], letter verbal fluency [17], or executive functions [7, 10, 13, 15, 16, 18].

BvFTD often impairs theory of mind (ToM) [19] which refers to the capacity to recognize and understand one's own or others' mental states, distinguishing those that have a basis in reality from persuasion, metaphor, lie, or delusion. This

ability contributes to predictions of others' behavior and to maintaining appropriate flexible social conduct [20, 21]. Therefore, it is likely that impaired ToM explains changes in personality and behavior in bvFTD or other neurodegenerative disorders [22]. The components of ToM are distinguished into the recognition of affective and epistemic mental states (e.g., knowledge, opinions, desires, and intentions) [23] . The amygdala [24, 25], prefrontal medial and inferior cortex [26, 27], orbital cortex [27, 28], superior temporal sulcus, temporoparietal junction [29], basal ganglia [30], and cerebellum [31] are linked to ToM, although the role played by each region remains unclear.

Compared with AD patients, bvFTD patients showed impairments at first- and second-order false beliefs, faux pas (FP) recognition, and eye reading, relating to frontal medial and dorsolateral atrophy, psychopathological symptoms, and perseverations [32]. Compared with healthy subjects, they were impaired at eye reading and FP tests involving emotion recognition [33] or at cartoon ToM tests [34], while, in comparison with primary aphasia patients, they were impaired in lie and joke-related tests, and these deficits correlated with social dilemma recognition [35]. In patients with bvFTD, ToM revealed consistent defects across different tasks and patient groups [19] and it was unrelated to other cognitive defects [36]. However, some neuroimaging and clinical analyses showed no association between ToM impairment and bvFTD [6]. Previous studies also suggested that ToM involves intelligence [37], memory [38], language [39], and executive functions [40] (i.e., working memory, maintaining crucial information online until the representation or interpretation of a mental state has been completed, and the inhibition of interference caused by reality and one's own perspective) [37, 38, 41–43], but, in patients with amygdala [24, 44] or frontal lobe damage [26, 28, 45], it was independent of executive deficits. Task content and demand may affect the performance, as the faux pas task (FPT) [28, 32, 46] is more difficult than other tests, while the use of shortened versions or summary scores in bvFTD patients means that some of ToM aspects are missed [32, 33].

In sum, bvFTD and ToM have common neuroanatomical substrates but the level of ToM, as expressed by task scores, showed inconsistent relationships with frontal lobe atrophy and did not clarify the epistemic and affective components or qualitative features of ToM. Still open questions include which components of ToM may be affected in bvFTD relating to particular areas of frontal lobe atrophy. This pilot study was aimed at determining qualitative features, analyzing the errors characterizing ToM impairment. Secondarily, we explored the relationship between these features and disease progression, the severity of dementia, and areas of prefrontal atrophy. We hypothesized that damage to the orbital cortex would impair the comprehension of mental states, while damage to the dorsolateral cortex would impair the ability to disengage one's own perspective from the factual context. ToM would be independent from other cognitive functions but is related to disease progression.

Method

Subjects

Fourteen patients with bvFTD [1, 4] were selected on the basis of concordant magnetic resonance imaging (MRI) findings [7], the absence of aphasia and psychiatric or brain-related disturbances, and an ability to cooperate in performing the tests. The Clinical Dementia Rating (CDR) [47] indicated various degrees of dementia. Fourteen healthy subjects with similar age ($t = 0.042$, $p = 0.96$), years of schooling ($t = 0.054$, $p = 0.95$), gender, and social background (urban, rural) were enrolled from the hospital visitors (Table 1).

Imaging

The signs of bvFTD on MRI were asymmetric frontal lobe atrophy in the ventromedial and dorsolateral prefrontal cortex, extending into the anterior-superior temporal lobe; atrophy of the anterior cingulated gyrus; atrophy of the head of the caudate nuclei (enlargement of the frontal horn of the lateral ventricle); and abnormal signal intensity in the subcortical white matter of the frontal and temporal lobes [7]. In accordance with Galton et al. [32] and Gregory et al. [48], all of the images were evaluated by visual analysis assigning a score of 0–4 proportional to the volume of the prefrontal cortical areas. The radiologist was unaware of the clinical diagnosis. The anatomical landmarks of the cortical areas were identified in accordance with Tamraz and Comair's guidelines [49]. The evaluation of the orbital area was made on MRI coronal cuts parallel to the posterior commissural-obex line, comprehended from the frontal pole to the level of the optic channel, and included the rectus and orbital gyri. The dorsolateral area was evaluated on sagittal cuts passing through the sylvian fissure, extending to the surface of the frontal lobe and insula; the posterior border of this region was the precentral sulcus and the cuts included the inferior, middle, and superior frontal gyri (Fig. 1).

Theory of mind assessment

The FPT [28] requires the recognition of FP in 20 stories, assessing competences that are usually demonstrated successfully by age 9–10 [28, 32]. It is more comprehensive than other tests because it requires distinguishing intentional and non-intentional actions and multiple perspectives, thus making it possible to determine the appreciation of false beliefs, emotional states, and intentions and the exclusion of false recognitions. Impaired attention and working memory could

Table 1 Subjects' demographic and clinical characteristics

	bvFTD patients	Healthy subjects
Females/males	6/8	6/8
Schooling (years)	11.14 ± 3.37 (8–17)	11.07 ± 3.58 (8–17)
Age	56.79 ± 14.92 (23–75)	56.57 ± 12.05 (29–73)
Disease duration (years)	2.71 ± 1.64 (1–7)	–
Clinical Dementia Rating	1.68 ± 0.53 (1–3)	–

Ranges appear in parentheses

bvFTD, behavioral variant frontotemporal dementia

interfere with patients' ability to hold a large amount of information in mind, while poor mental flexibility and excessive cohesiveness to the physical details of the story could undermine their ability to take another's perspective and to

Fig. 1 Magnetic resonance aspects of behavioral variant frontotemporal dementia. **a** Coronal fluid–attenuated inversion. Recovery (FLAIR) image at the level of the orbital frontal area shows cortical atrophy and mild abnormal signal intensity more pronounced in the rectus and orbital gyri on the left side. **b** Sagittal T1-weighted image at the level of the prefrontal dorsolateral region shows severe cortical atrophy in the inferior and middle frontal gyri

appreciate the social relations. For these reasons, we deviated from a prior synthetic FP approach that indicated the severity of the deficits but did not account for the possible effect of poor recall of contextual information, false recognitions, and the type of errors that may be revealed by detailed analysis of all comprehension responses [32, 33].

Each story was read aloud by the examiner, while the text remained in front of the subject who could read it again whenever necessary. After reading, the subjects were asked the recognition question: "Did anyone say something they shouldn't have said?" If they answered "yes," they were asked four comprehension questions ("Who said something they shouldn't have said?", "Why shouldn't he/she have said what he/she did?", "Why did he/she say that?", "How did he/she feel?") to assess their identifying the character making the FP, judging the behavioral inadequacy, distinguishing intentional behavior, and recognizing emotions. A control question was asked at the end of each story check in order to verify that the subject had understood the factual details. The FPT provided separate scores for recognition of the presence or absence of a FP, response to the comprehension questions, and awareness of the factual details; each score ranged from 0 to 10 (1 point attributed to each correct response); a total comprehension score was also computed.

The errors made by the bvFTD patients on the FPT stories were determined by evaluating their responses to the comprehension questions. Different errors were defined with reference to behavior aspects: poor comprehension, initiative and mental flexibility, flat affectivity, scarce or no adherence to reality, and paranoid-like inference such as self-projection into a story, suspicious comments, attribution of mental states that have no basis in reality, and cohesiveness to factual or physical details.

Other neuropsychological tests

The Digit and Corsi's Blocks span, short story, Token, phonemic and semantic word fluency, Raven's Colored Progressive Matrices, Tower of London, Weigl's Sorting, Trail Making B, and Attentive Matrices tests assessed verbal and visuospatial memory span, episodic memory, verbal comprehension, initiative and fluency, abstract reasoning, planning, set shifting, and attention [7].
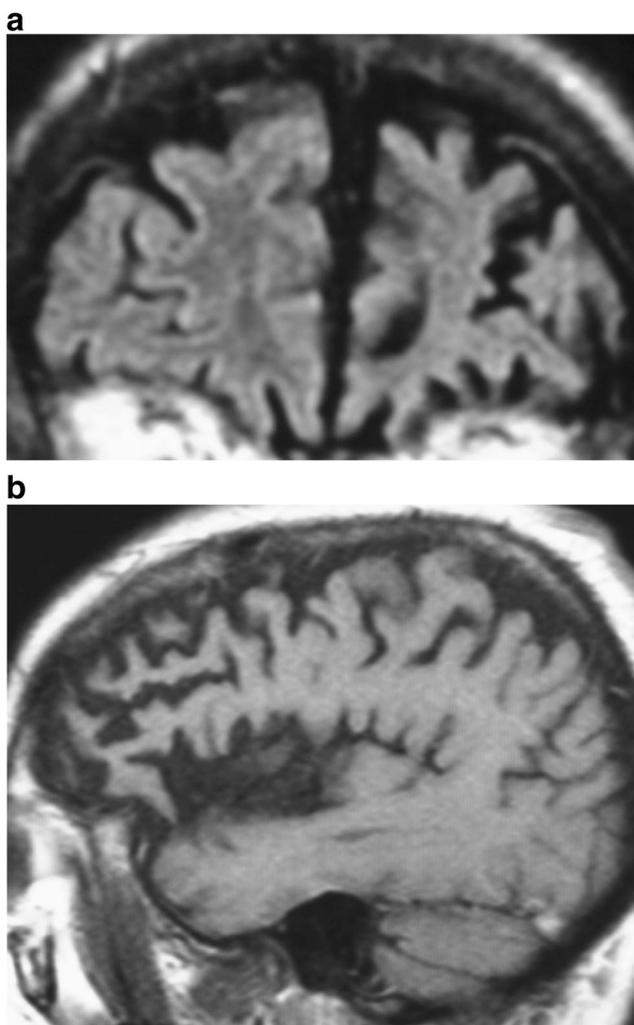
Data analysis

Given the exploratory nature of the study and necessity to look at the FPT in its entirety, all items were considered for examination of the study hypotheses. In order to determine the specificity of ToM performances, different analyses were used. The influence of the working memory was directly addressed by assessing the responses to the FPT control questions and comparing patients with normal (one or no incorrect response) or impaired control scores. The correlations between ToM and other cognitive functions were assessed by Spearman tests. Separate Mann-Whitney tests compared patients' and controls' FPT scores, setting the significance limit for six pairwise comparisons at $p \leq 0.008$ (Bonferroni's correction), and the other test scores, setting the significance limit for 11 pairwise comparisons at $p \leq 0.004$. The consistency of different errors with the FPT scores was assessed by the Spearman correlation. The demographic (age, schooling, gender) and disease-related variables (disease duration, CDR score, orbital and dorsolateral prefrontal atrophy) related to ToM were assessed by Spearman tests.

Results

Comparisons of neuropsychological performance

Compared with the controls, the bvFTD patients were significantly impaired at the neuropsychological tests, except for Digit span (Table 2).

With respect to the controls, the bvFTD patients were significantly impaired in FP recognition, comprehension of false beliefs, emotional mental states, and intentions and non-FP exclusion, and had lower FP and non-FP control scores (Table 3).

Correlations between theory of mind and other cognitive functions

In the bvFTD patients, the FP recognition and non-FP exclusion scores negatively correlated (rho = − 0.65, p = 0.012), whereas they showed no correlation with the comprehension scores. Mann-Whitney tests (U = 19 to 24, $p > 0.50$) confirmed the lack of a difference in ToM between the patients with normal FTP control scores (FP recognition 7.71 ± 2.21, first question 4.86 ± 2.41, second question 3.86 ± 2.54, third question 2.57 ± 2.22, fourth question 3.57 ± 2.99, non-FP exclusion 4.71 ± 3.40) and those with low FPT control scores (FP recognition 8.29 ± 1.38, first question 5.29 ± 2.69, second question 4.57 ± 2.52, third question 3.14 ± 3.43, fourth question 3.71 ± 2.98, non-FP exclusion: 6.00 ± 3.41). None of the FPT recognition or comprehension scores correlated with the control question scores (rho = 0.06 to 0.32, $p > 0.50$). There was a mild correlation between the second (rho = 0.61, p = 0.021) and fourth comprehension scores (rho = 0.57, p = 0.034) and semantic word fluency, and between the third comprehension score and short story (rho = 0.55, p = 0.043).

In the healthy control subjects, the FP recognition scores significantly correlated with the first (rho = 1, $p < 0.001$), second (rho = 0.74, p = 0.002), and fourth comprehension scores (rho = 0.63, p = 0.015), while the non-FP exclusion score had no significant correlation with the Digit span (rho = 0.55, p = 0.028) and Attentive Matrices scores (rho = 0.61, p = 0.02).

Table 2 Mean neuropsychological test scores in behavioral variant frontotemporal dementia patients and healthy subjects

Neuropsychological tests	bvFTD patients	Healthy subjects	Mann-Whitney tests
Raven's Colored Progressive Matrices (0–36)	22.57 + 5.01	31.21 + 4.35	$U = 20, p < 0.001$
Weigl's Sorting test (0–15)	5.50 + 2.63	11.36 + 2.24	$U = 8.5, p < 0.001$
Tower of London (0–36)	13.70 + 6.05	26.00 + 4.03	$U = 1, p < 0.001$
Trail Making test B	385.64 + 188.72	112.00 + 46.71	$U = 13.5, p < 0.001$
Attentive Matrices (0–69)	43.93 + 10.52	55.36 + 4.71	$U = 25, p = 0.001$
Word fluency (phonemic)	17.93 + 10.41	36.14 + 12.34	$U = 20, p < 0.001$
Word fluency (semantic)	22.14 + 9.55	40.50 + 6.12	$U = 11, p < 0.001$
Token test (0–36)	30.46 + 4.32	34.29 + 1.54	$U = 40, p = 0.007$
Digit span	5.29 + 0.99	6.07 + 1.07	NS
Corsi's Blocks span	4.07 + 1.07	5.57 + 0.85	$U = 28, p = 0.001$
Short story (0–28)	7.35 + 4.88	15.71 + 3.86	$U = 28, p = 0.001$

The neuropsychological tests column reports the score ranges (in parentheses) except for the tests that have no established maximum scores. Higher scores indicate better performances, except for Trail Making Tests A and B

bvFTD, behavioral variant frontotemporal dementia

Table 3 Mean faux pas task scores in behavioral variant frontotemporal dementia patients and healthy subjects

FPT performances	bvFTD patients	Healthy subjects	Mann-Whitney tests
FP recognitions	8.00 ± 1.79	9.71 ± 0.46	$U = 40, p = 0.004$
Non-FP exclusions	5.36 ± 3.34	9.79 ± 0.57	$U = 18.5, p < 0.001$
Comprehension question 1 "Who said something they should not have said?"	5.07 ± 2.46	9.71 ± 0.46	$U = 4, p < 0.001$
Comprehension question 2 "Why should not he/she have said what he/she did?"	4.21 ± 2.60	9.57 ± 0.64	$U = 3.5, p < 0.001$
Comprehension question 3 "Why did he/she say that?"	2.86 ± 2.79	8.93 ± 1.38	$U = 7.5, p < 0.001$
Comprehension question 4 "How did he/she feel?"	3.64 ± 2.87	9.50 ± 0.51	$U = 3.5, p < 0.001$
FP control questions	8.50 ± 1.91	10 ± 0.00	$U = 42, p = 0.001$
Non-FP control questions	8.79 ± 1.62	10 ± 0.00	$U = 35, p = 0.001$

bvFTD, behavioral variant frontotemporal dementia; *FP*, faux pas; *FPT*, faux pas task

Error analysis

The bvFTD patients correctly recognized an FP in 113 (81%) of the 140 FP stories and incorrectly attributed an FP (false recognition) in 53 (46%) of the 140 non-FP stories. The comprehension questions asked after presentation of these 166 stories identified the following errors: (a) non-response or incorrect person identification at the first question ("Who said something they shouldn't have said?") (e.g., an offense was attributed to the victim of the FP); (b) non-response or cohesiveness-related (i.e., an explanation based on factual or physical details, in the absence of attention to the social context) or delusional responses (i.e., redundant or abnormal interpretation of the events, with attribution of mental states in the absence of a basis in reality, such as attribution of non-existent bad intentions or fiendish aims) to the second ("Why shouldn't he/she have said what he/she did?") and third question ("Why did he/she say that?"); and (c) non-response or incorrect identification of emotions in reply to the fourth question ("How did he/she feel?"). The errors tallied by the examiner during the evaluation were blindly checked by another neuropsychologist, with 95% inter-rater agreement. The appendix presents some typical errors. Table 4 summarizes the distribution of different errors from the 113 FP stories.

There was high consistency, as an index of structural validity, between the qualitative errors and the FPT recognition

Table 4 Percentage of various error types committed by the behavioral variant frontotemporal dementia patients

Error types	FP stories	Non-FP stories
Incorrect person identification	41	100
Cohesiveness related	71	61
Delusional	48	46
Non-response	32	84
Incorrect emotion identification	59	100

FP, faux pas

and comprehension scores. Incorrect person identifications negatively correlated with three comprehension scores (first rho = − 0.66, p = 0.009; second rho = − 0.57, p = 0.03; fourth; rho = − 0.65, p = 0.01), the delusional responses to the second question with the second (rho = − 0.54, p = 0.047) and fourth question scores (rho = − 0.53, p = 0.05), the non-responses to the third question with all question scores (first rho = − 0.68, p = 0.007; second rho = − 0.65, p = 0.01; third rho = − 0.72, p = 0.003; fourth rho = − 0.66, p = 0.01), and the non-responses to the fourth question with the fourth question score (rho = − 0.53, p = 0.05).

The non-FP exclusion score was negatively associated with the number of incorrect person identifications (rho = − 0.98, p < 0.001). On the contrary, no type of FP error was associated with the FPT control question scores or other neuropsychological test scores.

Correlations of ToM impairments

Among the patients, the FPT recognition, exclusion, comprehension, and control scores did not show any relationship to the demographic or clinical variables, except for the first comprehension score which was negatively associated with disease duration (rho = − 0.55, p = 0.043).

For the FP stories, the number of delusional responses to the second question correlated with the degree of orbital prefrontal atrophy (rho = 0.64, p = 0.015) and disease duration (rho = 0.54, p = 0.044). For the FP and non-FP stories, the number of delusional responses to the third question correlated with the degree of orbital prefrontal atrophy (rho = 0.57, p = 0.032).

The number of cohesiveness-related responses to the second question correlated with age (rho = 0.66, p = 0.01) for the FP stories and with the degree of dorsolateral prefrontal (rho = 0.60, p = 0.025) for the non-FP stories. The total number of cohesiveness-related responses significantly correlated with the degree of dorsolateral prefrontal atrophy (rho = 0.60, p = 0.0023).

Discussion

This study analyzed the qualitative features of mental state attribution in bvFTD. The results suggest that ToM impairments represent a specific dysfunction related to disease progression.

ToM was marked by the attribution of non-existent mental states and altered comprehension of intentionality. Unlike healthy subjects, these patients showed no association between recognition and comprehension of mental states, highlighting that, even when they accurately recognized a FP, they could not appreciate intentionality, unintentionality, behavioral appropriateness, or affective tonality within a social context.

Qualitative analysis showing delusional and cohesiveness-related errors, person misidentification, and altered emotional state recognition, which are congruent with bvFTD-related behavior, may reflect different mechanisms. The delusional beliefs may indicate the attribution of mental states in the absence of a factual basis in reality or confusion between one's own and others' mental states, as these patients often projected the story contents into their own personal experience. Incorrect person identification reveals confusion about mental states and interpersonal relations. Impaired emotional states identification may reflect either an impairment in the general capacity to understand mental states or an alteration of emotion processing [25, 27]. These aspects are in keeping with the random interpretation of mental states in real-life contexts, self-centeredness, lack of attention concerning the situation of others, and poor social tact, which, especially in the early stages of bvFTD, may mistakenly lead to psychiatric diagnosis [6].

The cohesiveness-related errors may indicate poor ideation, abstraction, or mental flexibility, as they were closely related to the factual or physical aspects of the stories. Clinically, these patients often did not understand information as distinct from the immediate context or directly reacted to the external stimuli. This type of failure may correspond to an impaired disengagement from concrete situations, also expressed by compulsive utilization actions in the overt bvFTD stages. Therefore, the delusional responses appear to pertain to ToM and can be distinguished from the cohesiveness-related responses that more likely pertain to the executive domain. The non-responses may reflect specific ToM alterations or scarce initiative.

The delusional responses and altered identification of characters in the FP stories related to disease duration, suggesting a relationship between ToM impairment and disease progression. The delusional responses also related to the degree of orbital prefrontal atrophy, but showed no association with the dorsolateral prefrontal atrophy, strengthening the role played by the orbital prefrontal cortex in ToM [27, 28]. Moreover, our data specify that the orbital prefrontal cortex is important to one ToM competence: understanding if others' mental states correspond to reality. The cohesiveness-related responses correlated with the atrophy of the dorsolateral prefrontal cortex and age that are relevant to executive functions [38, 50].

Patients with and without difficulties in keeping in mind factual details of the FPT stories showed similar ToM impairments, suggesting that their attribution of mental states was independent from the working memory. Moreover, no type of ToM error or FPT scores related to the control question or other neuropsychological test scores indicated limited or no influence for set shifting, divided attention, planning, language, and memory on ToM. On the contrary, there was high consistency between the errors and the FP recognition and comprehension. These results provide evidence that ToM is a specific domain, as observed in Asperger's syndrome or amygdala or frontal lobe damage [24, 26, 28, 44, 45].

Given the problems inherent in testing multiple associations in a small patient sample, a number of chance results could be expected as false positives. This was addressed by strict selection criteria, non-parametric statistics, and adjusting the significance level in relation to the number of variables. Findings were reinforced by the use of matched controls and error analysis involving a large number of items. Strict diagnostic criteria and prototypical cerebral atrophy provided a reliable basis for brain-behavior correlations, cooperating to define ToM in typical bvFTD cases. A pathological control group (e.g., AD) could extend the qualitative analysis of ToM.

To conclude, in bvFTD, impaired ToM is multifaceted and proportional to disease progression. Being in line with clinical hallmarks, the results of error analysis expands the ToM pattern of this disorder. The qualitative analysis used in this study, showing aspects related to prefrontal atrophy, may be a basis to develop a neurocognitive model to be employed in patients with neurodegenerative disorders in which ToM impairment can occur.

References

1. Rascovsky K, Hodges JR, Knopman D, Mendez MF, Kramer JH, Neuhaus J, van Swieten JC, Seelaar H, Dopper EG, Onyike CU, Hillis AE, Josephs KA, Boeve BF, Kertesz A, Seeley WW, Rankin KP, Johnson JK, Gorno-Tempini ML, Rosen H, Prioleau-Latham CE, Lee A, Kipps CM, Lillo P, Piguet O, Rohrer JD, Rossor MN, Warren JD, Fox NC, Galasko D, Salmon DP, Black SE, Mesulam M, Weintraub S, Dickerson BC, Diehl-Schmid J, Pasquier F, Deramecourt V, Lebert F, Pijnenburg Y, Chow TW, Manes F,

Grafman J, Cappa SF, Freedman M, Grossman M, Miller BL (2011) Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. Brain 134:2456–2477. https://doi.org/10.1093/brain/awr179

2. Neary D, Snowden JS, Northen B, Goulding PJ (1998) Dementia of frontal lobe type. J Neurol Neurosurg Psychiatry 51:353–361

3. Johnson JK, Diehl J, Mendez MF, Neuhaus J, Shapira JS, Forman M, Chute DJ, Roberson ED, Pace-Savitsky C, Neumann M, Chow TW, Rosen HJ, Forstl H, Kurz A, Miller BL (2005) Frontotemporal lobar degeneration. Arch Neurol 62:925–930

4. Leyton CE, Hodges JR (2010) Frontotemporal dementias: recent advances and current controversies. Ann Indian Acad Neurol 13:S74–S80

5. Schroeter ML, Raczka K, Neumann J, von Cramon DY (2007) Neural networks in frontotemporal dementia – a meta-analysis. Neurobiol Aging 36:497–510

6. Schroeter ML, Lair AR, Chwiesko C, Deuschl C, Scheiner E, Bzdok D, Eickhoff SB, Neumann J (2014) Conceptualizing neuropsychiatric diseases with multimodal data-driven meta-analyses. The case of behavioral variant frontotemporal dementia. Cortex 57:22–37

7. Giovagnoli AR, Erbetta A, Reati F, Bugiani O (2008) Differential neuropsychological patterns in frontotemporal dementia and Alzheimer's disease in a study of diagnostic concordance. Neuropsychologia 46:1495–1504

8. Frisoni GB, Pizzolato G, Geroldi C, Rossato A, Bianchetti A, Trabucchi M (1995) Dementia of the frontal type: neuropsychological and [99Tc]-HMPAO SPECT features. Int Ger Psychiat Neurol 8:42–48

9. Gregory CA, Orrell M, Sahakian B, Hodges J (1997) Can frontotemporal dementia and Alzheimer's disease be differentiated using a brief battery of tests? Int J Geriatr Psychiatry 12:375–383

10. Hodges JR, Patterson K, Ward R, Garrard P, Bak T, Perry R, Gregory C (1999) The differentiation of semantic dementia and frontal lobe dementia (temporal and frontal variants of frontotemporal dementia) from early Alzheimer's disease: a comparative neuropsychological study. Neuropsychology 13:31–40

11. Mendez MF, Cherrier M, Perryman KM, Pachana N, Miller BL, Cummings JL (1996) Frontotemporal dementia versus Alzheimer's disease: differential cognitive features. Neurology 47:1189–1194

12. Pachana NA, Boone BK, Millar BL, Cummings JL, Berman N (1996) Comparisons of neuropsychological functioning in Alzheimer's disease and frontotemporal dementia. J Int Neuropsychol Soc 2:505–510

13. Pasquier F, Lebert F, Grymonprez L, Pettit H (1995) Verbal fluency in dementia of frontal lobe type and dementia of Alzheimer type. J Neurol Neurosurg Psychiatry 58:81–84

14. Thompson JC, Stopford CL, Snowden JS, Neary D (2005) Qualitative neuropsychological performance characteristics in frontotemporal dementia and Alzheimer's disease. J Neurol Neurosurg Psychiatry 76:920–927

15. Walker AJ, Meares S, Sachdev PS, Brodaty H (2005) The differentiation of mild frontotemporal dementia from Alzheimer's disease and healthy aging by neuropsychological tests. Int Psychogeriatr 17:57–68

16. Siri S, Benaglio I, Frigerio G, Binetti G, Cappa SF (2001) A brief neuropsychological assessment for the differential diagnosis between frontotemporal dementia and Alzheimer's disease. Eur J Neurol 8:125–132

17. Perri R, Koch G, Carlesimo et al (2004) Alzheimer's disease and frontal variant of frontotemporal dementia. J Neurol 10:1238–1244

18. Davies RR, Hodges JR, Kril JJ, Patterson K, Halliday GM, Xuereb JH (2005) The pathological basis of semantic dementia. Brain 128:1984–1995

19. Henry JD, Phillips LH, von Hippel C (2014) A meta-analytic review of theory of mind difficulties in behavioural-variant frontotemporal dementia. Neuropsychologia 56:53–62

20. Shamay-Tsoory SG, Harari H, Aharon-Peretz J, Levkovitz Y (2010) The role of the orbitofrontal cortex in affective theory of mind deficits in criminal offenders with psychopathic tendencies. Cortex 46:668–677

21. Völlm BA, Taylor ANW, Richardson P, Corcoran R, Stirling J, McKie S, Deakin JF, Elliott R (2006) Neuronal correlates of theory of mind and empathy: a functional magnetic resonance imaging study in a nonverbal task. Neuroimage 29:90–98

22. Giovagnoli AR, Parente A, Villani F, Franceschetti S, Spreafico R (2013) Theory of mind and epilepsy: what clinical implications? Epilepsia 54:1639–1646

23. Giovagnoli AR (2015) The importance of theory of mind in epilepsy. Epilepsy Behav 39:145–153

24. Shaw P, Lawrence EJ, Radbourne C, Bramham J, Polkey CE, David AS (2004) The impact of early and late damage to the human amygdala on "theory of mind" reasoning. Brain 127:1535–1548

25. Stone VE, Baron-Cohen S, Keane J, Young A (2003) Acquired theory of mind impairments in individuals with bilateral amygdala lesions. Neuropsychologia 41:209–220

26. Rowe AD, Bullock PR, Polkey CE, Morris RG (2001) "Theory of mind" impairments and their relationship to executive functioning following frontal lobe excisions. Brain 124:600–616

27. Stuss DT, Gallup GG Jr, Alexander MP (2001) The frontal lobes are accessory for "theory of mind". Brain 124:279–286

28. Stone VE, Baron-Cohen S, Knight RT (1998) Frontal lobe contributions to theory of mind. J Cogn Neurosci 10:640–656

29. Saxe R, Wexler A (2005) Making sense of another mind. Neuropsychologia 43:1391–1399

30. Bodden ME, Dodel R, Kalbe E (2010) Theory of mind in Parkinson's disease and related basal ganglia disorders: a systematic review. Mov Disord 25:13–27

31. Parente A, Manfredi V, Tarallo A, Salsano E, Erbetta A, Pareyson D, Giovagnoli AR (2013) Selective theory of mind impairment and cerebellar atrophy: a case report. J Neurol 260:2166–2169

32. Gregory C, Lough S, Stone V, Erzinclioglu S, Martin L, Baron-Cohen S, Hodges JR (2002) Theory of mind in patients with frontal variant frontotemporal dementia and Alzheimer's disease: theoretical and practical implications. Brain 125:752–764

33. Torralva T, Kipps CM, Hodges JR, Clark L, Bekinschtein T, Roca M, Calcagno ML, Manes F (2007) The relationship between affective decision-making and theory of mind in the frontal variant of fronto-temporal dementia. Neuropsychologia 45:342–349

34. Lough S, Kipps CM, Treise C, Watson P, Blair JR, Hodges JR (2006) Social reasoning, emotion and empathy in frontotemporal dementia. Neuropsychologia 44:950–958

35. Eslinger PJ, Moore P, Troiani V, Antani S, Cross K, Kwok S, Grossman M (2007) Oops! Resolving social dilemmas in frontotemporal dementia. J Neurol Neurosurg Psychiatry 78:457–460

36. Ramanan S, de Souza LC, Moreau N, Sarazin M, Teixeira AL, Allen Z, Guimarães HC, Caramelli P, Dubois B, Hornberger M, Bertoux M (2017) Determinants of theory of mind performance in Alzheimer's disease: a data-mining study. Cortex 88:8–18. https://doi.org/10.1016/j.cortex.2016.11.014

37. Samson D, Apperly IA, Humphreys GW (2007) Error analysis reveal contrasting deficits in "theory of mind": neuropsychological evidence from 3-option false belief task. Neuropsychologia 45:2561–2569

38. Maylor EA, Moulson JM, Muncer AM, Taylor LA (2002) Does performance on theory of mind tasks decline in old age? Br J Psychol 93:465–485

39. Surian L, Siegal M (2001) Sources of performance on theory of mind tasks in right hemisphere-damaged patients. Brain Lang 78:224–232

40. Bibby H, McDonald S (2005) Theory of mind after traumatic brain injury. Neuropsychologia 43:99–114

41. Carlson SM, Moses LJ (2001) Individual differences in inhibitory control and children's theory of mind. Child Dev 72:1032–1053

42. McKinnon MC, Moscovitch M (2007) Domain-general contributions to social reasoning: theory of mind and deontic reasoning re-explored. Cognition 102:179–218

43. Channon S, Crawford S (2002) The effects of anterior lesions on performance on a story comprehension test: left anterior impairment on a theory of mind-type task. Neuropsychologia 38:1006–1017

44. Fine C, Lumsden J, Blair RJR (2001) Dissociation between "theory of mind" and executive functions in a patient with early left amygdala damage. Brain 124:287–298

45. Bird CM, Castelli F, Malik O, Frith U, Husain M (2004) The impact of extensive medial frontal lobe damage on "theory of mind" and cognition. Brain 127:914–928

46. Baron-Cohen S, O'Riordan M, Stone V, Jones R, Plaisted K (1999) Recognition of faux pas by normally developing children and children with Asperger syndrome or high-functioning autism. J Autism Dev Disord 29:407–418

47. Hughes CB, Berg L, Danzinger WL (1982) A new clinical scale for the staging of dementia. Br J Psychiatry 140:566–567

48. Galton CJ, Patterson K, Xuereb JH, Hodges JR (2000) Atypical and typical presentation of Alzheimer's disease: a clinical, neuropsychological, neuroimaging and pathological study of 13 cases. Brain 123:484–498

49. Tamraz JC, Comair YG (2000) Atlas of regional anatomy of the brain using MRI with functional correlation. Springer-Verlag Berlin Heidelberg, New York, pp 1–330

50. Jurado MB, Rosselli M (2007) The elusive nature of executive functions. Neuropsychol Rev 17:213–233