In two minds - executive functioning vs. theory of mind in behavioural variant frontotemporal dementia

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Abstract

Background: The relationship of executive function (EF) and theory of mind (ToM) deficits in neurodegeneration is still debated. There is contradicting evidence as to whether these cognitive processes are overlapping or distinct, which has clear clinical relevance for the evaluation of their associated clinical symptoms.

Aim: To investigate the relationship of EF and ToM deficits via a data-driven approach in a large sample of behavioural variant frontotemporal dementia patients (bvFTD).

Methods: Data of forty-six bvFTD patients was employed in a hierarchical cluster analysis to determine the similarity of variance between different EF measures (verbal abstraction, verbal initiation, motor programing, sensitivity to interference, inhibitory control, visual abstraction, flexibility, working-memory/attention) and ToM (faux-pas).

Results: Overall results showed that EF measures were clustered separately from the ToM measure. A post-hoc analysis revealed a more complex picture where selected ToM sub-components (empathy; intention) showed a relationship to specific EF measures (verbal abstraction; working-memory/attention), whereas the remaining EF and ToM sub-components were separate.

Conclusion: Taken together, these findings suggest that EF and ToM are distinct components, however ToM empathy and intention sub-components might share some functions with specific EF processes. This has important implications for guiding diagnostic assessment of these deficits in clinical conditions.

Introduction

Executive functions (EF) and theory of mind (ToM) are two crucial cognitive domains to produce adaptive social behaviour. Although both domains have been extensively studied separately, it is still not clear whether or how they interact. This is particularly relevant for neurodegenerative disease, such as behavioural variant frontotemporal dementia (bvFTD), which can present with deficits in both EF and ToM,[1] though it is not clear whether one is dependent on the other. This is of importance as classically, EF deficits showed a poor relationship with the florid neuropsychiatric symptoms in bvFTD, suggesting that EF deficits might be less relevant in causing neuropsychiatric dysfunction than ToM deficits.

Previous studies investigating the relationship of EF and TOM in bvFTD have yielded variable results, either supporting a complete dissociation,[2, 3] or a dependency between EF and ToM.[4] One particular problem with the previous approaches was that they employed binomial correlation analyses or ANOVA, which do not test directly the dependency of factors with each other. Cluster analysis, by contrast, is a technique that allows investigating the relationship between cognitive measures more directly.

To investigate the relationship between EF and ToM in the current study we took a two-step procedure involving binomial correlations and hierarchical cluster analysis to determine the similarity of variance between EF and ToM. We hypothesised to find converging evidence across analyses techniques showing that ToM impairments are relatively independent from EF in bvFTD.

Methods

Participants

Forty-six bvFTD patients were selected from the database of the Memory and Alzheimer Institute of the Pitié-Salpêtrière hospital from 2007 to 2012. Patients fulfilled consensual diagnostic criteria for bvFTD.[5] We included patients with memory impairment if the other core diagnostic criteria of bvFTD were present. All patients were followed at least 24 month in an expert FTD centre to increase the clinical confidence of the diagnosis. We did not include participants who presented with evidence of focal lesions, severe cortical or subcortical vascular lesions, severe depression, or motor neuron disease. Patients had a mean score on the Mini Mental State Examination of 24.5 (±3.7), a mean score on the Mattis' Dementia Rating Scale of 126.4 (±11.7),[6] a mean score on the Frontal Assessment Battery (FAB) of 13.2 (±3.2).[7] Biological and clinical data were generated during routine clinical workups and were retrospectively extracted for the purpose of this work. According to French legislation, explicit informed consent was waived, as patients and their relatives were informed that individual data might be used in retrospective clinical research studies.

EF and ToM assessments

All patients underwent a set of executive tests including the FAB, the modified Wisconsin Card Sorting Test (mWCST),[8] and digit spans forward and backward. Five sub-scores of the FAB were analysed: similarities, verbal (lexical) fluency, motor-sequences, conflicting instructions and Go/No-go. The grasping subscore was excluded from the analyses, as this is a behavioural sign. Patients also underwent the modified faux pas test included in the reduced Social cognition and Emotional Assessment (mini-SEA),[9] which evaluates theory of mind through short stories that contain, or not, a social faux-pas. In this test, patients have to detect the presence of a faux pas (detection) and answer questions assessing the attribution of the faux pas to a character of the story, its identification, knowledge and intentionality, as well as its emotional impact on a victim (empathy).

Statistical analyses

Correlations analyses, using Spearman coefficient, were conducted. To determine how closely EF and ToM measures were related, a hierarchical cluster analysis (Ward's method) was performed. Data were first standardized (z-scores). During the analysis, each variable was defined as an individual cluster. Clusters were then sequentially merged according to their similarity, or distance (squared Euclidean distance) in a geometric space where the number of variables set the number of dimensions. A dendrogram, or branching diagram, was then computed to represent the relationships of similarity among the group of variables.

Results

Correlations are presented in table 1. There was no significant correlation between the faux-pas test and EF measures after Bonferroni's correction for multiple comparisons, while significant correlations were observed between EF measures.

	Verbal fluency	Similarities	Motor Sequences	Conflicting Instructions	Go/NoGo	Digit Span Forward	Digit Span Backward	Faux-Pas
mWCST	0.51*	0.41	0.11	0.16	0.22	0.31	0.31	0.11
Verbal fluency		0.35	0.20	0.32	0.23	0.49 *	0.49 *	-0.16
Similarities			0.08	0.21	0.32	0.37	0.57 *	0.32
Motor Sequences				0.16	0.52 *	0.24	0.25	-0.35
Conflicting Instructions					0.28	0.22	0.19	0.08
Go/NoGo						0.23	0.38	-0.13
Digit Span Forward							0.73 *	0.01
Digit Span Backward								0.11

Table 1 – Coefficient matrix including executive functioning and theory of mind measures. WCST= modified Wisconsin Card Sorting Test.
* = p<0.005 (corrected for multiple comparison)

The hierarchy resulting from clustering the data is shown in the figure 1A. On this dendrogram, similar variables are joined at an early stage of the analysis (at the bottom of the dendrogram) and less similar variables are joined at later stages (at the top). Two clusters were recognised by the analysis, identified by marked discontinuity, or "step" in the hierarchy. Similarities, verbal fluency, motor-sequences, conflicting instructions, Go/No-go, digit span backward and forward as well as mWCST formed one distinct cluster (a). By contrast, the score of the Faux-pas test formed a single and distinct cluster (b).

A *post-hoc* analysis was performed on a subgroup of patients (n=17) in order to investigate the differential link between ToM subcomponents and EF. Three distinct clusters were identified (Figure 1B): (a) a 'pure' executive cluster, including mWCST, verbal fluency, motor-sequences, conflicting instructions, Go/No-go; (b) a ‘pure’ ToM cluster composed of the detection, attribution, identification and knowledge subscores of the faux pas test; and (b) a ‘mixed’ cluster including the intention and empathy subscales of the faux-pas test as well as similarities and digit span test scores.

Discussion

This study investigated the relationship between EF and ToM in bvFTD. Using a statistical clustering approach, we showed that ToM, as measured by the faux pas test, was independent from EF performance. Furthermore, when the subcomponents of the faux pas test were considered separately, we observed that the majority of ToM components clustered together, independently from a core EF cluster. In contrast, the intention and empathy ToM components were linked to attention/working-memory and verbal abstraction performance. Together, these results suggest a different relationship with EF across ToM components.

In more detail, for the performance of the faux pas and EF measures, the dendrogram (figure 1A) showed two distinct clusters: (1) an “executive” cluster including measures of verbal abstraction (similarities), verbal initiation (fluency), motor programing (motor-sequences), sensitivity to interference (conflicting-instructions), inhibitory control (Go/No-go), visual abstraction/flexibility (mWCST) and working-memory/attention (digit spans); and (2) a cluster solely composed of ToM (faux-pas).

This is in stark contrast to developmental studies that often reported correlations between EF and ToM, and led authors point to a parallel development of both functions.[10] Similar empirical evidence is derived from psychopathology, where the co-occurrence of EF and ToM impairments is frequently observed in autism or attention deficit with hyperactivity disorder.[11, 12] However, only a few studies investigated this relationship in neurodegeneration, although EF and ToM deficit are frequently observed together, especially in bvFTD. The independence between ToM and EF in bvFTD was originally suggested by Lough and colleagues,[13] who described the case of a 47-year-old patient presenting a relatively intact EF assessment but a strong deficit in several ToM tasks. Using correlation or

ANOVA approaches, more recent group-studies replicated this dissociation.[2, 3] By contrast, others results supported the idea that ToM and EF were significantly linked,[4] which led some authors to consider ToM impairments as part of a cognitive dysexecutive syndrome.[14] While the cluster architecture shown in our study supports the existence of a cognitive dysexecutive syndrome, it strongly suggests that ToM and EF are largely independent. This result could be put in perspective with recent findings highlighting a strong dependency of EF on fluid intelligence - both involving a common dorsal and lateral prefrontal network - although, by contrast, ToM does not seem to depend solely on the level of fluid intelligence and is dependent from a more medial prefrontal network.[15]

There are some limitations to the current study, including the limited sample size for the *post-hoc* analysis, which needs to be replicated on lager sample. Also, we use a single test to assess ToM, although it is a complex function, involving multiple sub-processes. However, we used a modified version of the faux pas test, which requires the detection and interpretation of social indiscretions and which is the only test allowing an evaluation of the different ToM processes. When the different subcomponents of the faux pas test were considered separately (figure 1B), we observed that the detection, attribution, identification and knowledge of faux pas clustered together, distinctively from a core executive cluster composed from most of the EF scores. A third and more mixed cluster was composed from measures of attention, working memory and verbal abstraction as well as scores of mental states attribution (empathy and intention) from the faux pas test. In line with a previous study,[16] these results suggest that, while ToM is independent from EF, EF support some specific ToM subcomponents, such as mental-state attribution. False belief, ‘reading the mind in the eyes’ or faux pas tests have indeed different psychometric properties and involve different ToM subcomponents.[17] Although we believe that ToM is a distinct module, other cognitive functions such as semantic (e.g. social rules or conventions), or episodic memory (e.g. previous similar experience), could also have an effect on ToM processing. In an attempt to deconstruct ToM into sub-processes and to investigate their relationship with EF, our findings show a complex relationship that illustrate the need to explore ToM further in order to know whether it relies on a dedicated processing mechanism, with EF acting as supportive but distinct processes, or if ToM depends on unspecific perceptive, attentional and executive processes.[18]

Finally, the present study highlights the lack of power of binomial correlation methods to identify similarities beyond an entire group of variables. Significant correlations were not observed between EF and ToM measures while they were observed within different executive scores. However, correlations within the different executive scores were far from systematic. In addition, when considering the correlation-coefficient as an effect-size, the link between EF and ToM as well as the link between the different EF scores are both difficult to interpret. On the sole basis of this result, it would be difficult to draw conclusions about the relationship of EF and ToM. In contrast, the dendrogram resulting from the cluster analysis shows clearly how ToM is distinct from EF measures, which are all grouped in a single cluster (Figure 1A). Consequently, we believe that while strong conclusions could be derived from a correlation analysis employed to investigate the relationship between several variables, a more comprehensive approach is needed on larger data sets, such as the current study. Our findings highlight that data-mining techniques, using clustering or factors analyses to find and visualise natural grouping of patterns in data, should be employed more extensively in clinical neurosciences. Such approaches would complement the more classic comparison or correlation analyses, and could also be used to map clusters or factors to the brain atrophy in neurodegeneration.

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Competing interests

The authors have no competing interests to disclose.

Authors contribution

MB: design, clinical and experimental data acquisition, statistical analysis and interpretation and manuscript writing.

CO: interpretation and manuscript writing.

BD: clinical data acquisition, manuscript revision.

MH: design, interpretation and manuscript writing.

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Figure 1 legend

Dendrogram using Ward's linkage, showing the cluster architecture of EF and ToM (A) and of EF and ToM subcomponents (B). DF: Digit Span Forward; DB: Digit Span Backward; SIM: Similarities; WCST: Wisconsin Card Sorting Test; VF: Verbal fluency; CI: Conflicting Instructions; MoS: Motor Sequences; GNG: Go/NoGo; FP: faux pas. INT: Intention; EMP: Empathy; DET: Detection; ATB: Attribution; ID: Identification; KNO: Knowledge.