Neuropsychologia ■ (■■■■) ■■■–■■■

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

A meta-analytic review of theory of mind difficulties in behavioural-variant frontotemporal dementia

Q1 Julie D. Henry [a,*], Louise H. Phillips [b], Courtney von Hippel [a]

Q3 [a] School of Psychology, University of Queensland, St. Lucia, QLD 4072, Australia
[b] School of Psychology, University of Aberdeen, United Kingdom

ARTICLE INFO

Article history:
Received 21 June 2013
Received in revised form
13 December 2013
Accepted 31 December 2013

Keywords:
Frontotemporal dementia
Theory of mind
Social cognition
Quantitative review

ABSTRACT

Theory of mind (ToM) refers broadly to our understanding of others' complex emotions and mental states. Deficits in ToM are widely regarded as one of the key defining features of the behavioural variant of frontotemporal dementia (bvFTD), which is unsurprising given the key role that frontal and temporal neural systems are considered to play in mental state decoding. Here we report the first meta-analysis of this literature, providing a timely summary of the breadth, magnitude and specificity of ToM difficulties in this population. Across 15 datasets involving 800 participants (312 with bvFTD and for comparative purposes, 325 non-clinical controls and 163 participants with Alzheimer's disease), several key results emerged. Collapsed across all types of task, people with bvFTD performed more poorly than non-clinical controls, with the degree of ToM difficulty they experienced large in magnitude ($r = -.60$). These deficits were greater than those observed on control tasks matched to the ToM task in their general cognitive demands, but which can be solved without any mentalistic inference. BvFTD-related ToM difficulties were also significantly larger than the ToM difficulties seen in people with Alzheimer's disease. However, ToM difficulties in people with bvFTD were of a similar magnitude to the difficulties seen on measures of more basic social cue perception (emotion recognition). These data have important implications for understanding the types of ToM difficulties associated with bvFTD.

1. Introduction

Behavioural variant frontotemporal dementia (bvFTD) is a chronic neurodegenerative disorder characterised by changes in personality and interpersonal conduct, loss of empathy, increased stereotypic behaviours, disinhibition and emotion dysregulation (Hodges, 2013; Neary, Snowden, & Mann, 2005). These clinical symptoms and behavioural changes have mostly been related to progressive degeneration of the prefrontal and anterior temporal neocortex. Individuals diagnosed with bvFTD often show poor insight into these changes, and although deficits on neuropsychological measures of executive function may be seen, they often perform normally on standard assessments of cognitive function. As a consequence, there has been particular focus in the bvFTD literature on the need to identify alternative methods that might aid with initial diagnosis, as well as to provide a means of sensitively charting changes in social conduct over time. Attention has increasingly turned towards theory of mind (ToM), which is considered by some to be a potentially important prognostic indicator in this group.

ToM is a social cognitive skill that refers broadly to our capacity to understand others' mental states, and to appreciate that these may differ from our own (Premack & Woodruff, 1978). Difficulties reasoning about another's beliefs, feelings, desires, intentions or goals have clear and important consequences in clinical groups for whom social deficits profoundly limit functional capacity and quality of life. Previous research has shown that ToM imposes particular demands on the neural regions known to be affected in bvFTD. In particular, the medial prefrontal cortex (MPFC), lateral prefrontal cortex (LPFC) and temporal–parietal junction (TPJ) are core neural substrates involved in ToM operations (Carrington & Bailey, 2009). For example, Sommer, Döhnel, Sodian, Meinhardt, Thoermer and Hajak (2007) used a cartoon ToM task along with functional magnetic resonance imaging (fMRI) and found that false belief trials preferentially activated the right hemisphere TPJ, dorsal anterior cingulate cortex and left hemisphere LPFC relative to true belief trials, suggesting these regions play an important roles in the explicit registration of other's beliefs. It is therefore unsurprising that over the past decade considerable research attention has focused on clarifying exactly how ToM is affected in bvFTD. A recent qualitative review concluded that on measures of ToM, studies involving bvFTD patients, "found a common severe deficit." (p. 10, Poletti, Enrici, & Adenzato, 2012). Moreover, Pardini et al. (2013) notes that, "ToM deficits… have been proposed as the possible cognitive substrate of some of the key clinical features of bvFTD".

* Corresponding author. Tel.: +61 4 33656737; fax: +61 7 33654466.
E-mail address: Julie.henry@uq.edu.au (J.D. Henry).

0028-3932/$ - see front matter © 2014 Published by Elsevier Ltd.
http://dx.doi.org/10.1016/j.neuropsychologia.2013.12.024

However, as Le Bouc et al. (2012) note, "a number of studies have investigated the hypothesis of theory of mind deficit in behavioural variant FTD but have given rise to controversial results and conclusions" (p. 3027). Thus, although individuals with bvFTD do consistently perform poorly on measures of ToM, questions have been raised about the extent and specificity of these difficulties. Some studies have shown that individuals with bvFTD perform more poorly on measures of ToM than people with other neurodegenerative diseases (for a qualitative review, see Adenzato, Cavallo, & Enrici, 2010). For instance, in a study involving clinical participants with four different neurodegenerative diseases, Shany-Ur et al. (2012) concluded that while people with bvFTD demonstrated uniquely severe and focal ToM deficits at every level, in the other clinical groups ToM impairment appears to be driven by more general cognitive difficulties.

Contrasting with these findings, however, other studies have shown that measures of this construct are not specifically or disproportionately disrupted in bvFTD relative to more common neurodegenerative conditions such as Alzheimer's disease (Fernandez-Duque, Baird, & Black, 2009; Fernandez-Duque, Hodges, Baird, & Black, 2010). Fernandez-Duque et al. (2009) showed that individuals with bvFTD and AD who were cognitively matched performed at ceiling on a first-order false-belief task, but were comparably impaired on a more cognitively challenging second-order false belief task. They concluded that the results, "pose a challenge to the claim that FTD-b's deficit in theory-of-mind reasoning is due to a conceptual deficit in mentalizing" (p. 494). Fernandez-Duque et al. (2010) also showed that individuals with bvFTD and AD presented with a very similar profile of impairment on a measure that required inferring what other people are feeling. While both clinical groups performed comparably to controls when emotions were displayed unambiguously and consistently, impairment was evident when these conditions were not met. It was argued that, "cognitive deficits can lead to impaired empathy even in patients who do not display obvious social deficits" (p. 296). However, contrasting with these findings, Freedman, Binns, Black, Murphy, & Stuss (2013) recently showed that both individuals with bvFTD and AD were significantly impaired on a measure of ToM – and that, for both of these groups, difficulties were not simply secondary to more general cognitive decline. Taken together, current literature does not provide a clear consensus on whether the ToM deficits seen in bvFTD are disproportionate to those associated with other neurodegenerative conditions, and in particular, AD, as well as the specificity of these deficits.

Finally, as noted, ToM is a complex social skill involving *reasoning* about mental states, which is dependent on more basic social perception such as decoding emotional cues to understand what mental states such as feelings are present. The extent to which the ToM deficits seen in bvFTD are in excess of these more basic social perceptual difficulties remains unclear. The most widely used measures of basic social perception assess the ability to identify facial expressions of emotions from photographs or vocal expressions from auditory cues. Several studies have now shown that individuals with bvFTD have significant deficits in decoding both facial (Bertoux et al., 2012) and vocal (Shany-Ur et al., 2012) expressions of emotion. Few bvFTD studies have directly compared the relative magnitude of deficits on measures of basic social perception and ToM, but this question has important implications for understanding the specificity of any ToM difficulties in this group.

1.1. Research questions and predictions

The present article is, to our knowledge, the first to use meta-analytic techniques to assess the effect of bvFTD on ToM. Meta-analytic techniques have the important advantages of allowing corrections for sampling error. Thus, in the present study it will be possible to assess whether discrepancies between studies reflect the influence of substantive factors, or artefactual variance. Indeed, since there is a tendency for sample size to be relatively small in clinical studies of this type, this area of research is especially susceptible to reification of sampling error, the most serious source of artefactual variance. However, it is not possible to correct for this artefact at the level of the individual study (Hunter & Schmidt, 1994).

Our quantitative review will help answer four main questions. First, a meta-analytic integration of this literature will provide important point estimates that will clarify the breadth and magnitude of any ToM difficulties in bvFTD. Secondly, the results will help clarify whether ToM deficits reflect a general or more specific impairment among individuals with bvFTD. This issue will be assessed by comparing the magnitude of ToM deficits to the deficits seen on control tasks which are matched to the ToM task in their general cognitive demands, but which can be solved without any mentalistic inference. Third, the results will establish whether the magnitude of ToM difficulties for individuals with bvFTD are in excess of those seen for individuals with AD, helping clarify recent controversies about whether ToM skills are subject to general impairment in different neurodegenerative conditions. Finally, we will compare the magnitude of bvFTD-related ToM deficits to those seen on measures of basic social perception (emotion recognition). Again, this latter question has important implications for understanding the specificity of any bvFTD–ToM related impairment.

2. Material and methods

2.1. Literature search

A systematic review of the existing research literature was conducted. Identification of studies eligible for inclusion was achieved by searching the *Web of Science* (Thomson Reuters), *Psych INFO* (American Psychological Association), and *Google-Scholar* (Google) databases. The key search parameters were: 'cognitive empathy', 'empathy', 'theory of mind', 'mentalising/mentalizing', 'false belief' and 'perspective taking', 'TASIT', 'MIET', 'MIET-R', 'Eyes' 'Happe's', 'Strange Stories', 'Faux pas/faux pax', coupled with 'frontotemporal dementia', ' dementia', 'frontotemporal', 'frontal variant' and 'FTD'. Backward citation searches were also undertaken. The search was completed in June 2013.

2.2. Inclusion criteria

Studies were included if they (1) had a research design that compared participants with bvFTD to a healthy age-matched comparison group. For all included studies, bvFTD diagnoses were made according to accepted international consensus criteria (McKhann et al., 2001; Neary et al., 1998; Rascovsky et al., 2011), while healthy was defined as the absence of serious psychiatric or neurological illness. Two studies were excluded due to the absence of non-clinical control data (Mendez & Shapira, 2011; Pardini et al., 2013), and one (Roca et al., 2013) due to reporting a re-analysis of an earlier dataset that already contributed to the meta-analysis. In a further study, only control data from a separate study already included in the meta-analysis was available, and consequently was not included (Bertoux et al., 2012). Single case studies were also not included in this meta-analysis (Lough, Gregory, & Hodges, 2001; Lough & Hodges, 2002; Poletti, Borelli, & Bonuccelli, 2011). Additional inclusion criteria were that each study must have (2) been written in English, and (3) presented precise statistics convertible to effect sizes. For studies that did not present all necessary statistics, authors were contacted directly to request the necessary data. Of these studies, only one was not included because the data needed to derive precise effect sizes was not reported in the manuscript and was not available due to relocation of the first author (Kipps, Nestor, Acosta-Cabronero, Arnold, & Hodges, 2009).

The final key criterion was that studies had to (4) include a behavioural measure of ToM with a primary focus on mental state attribution. Consequently, self-report tasks were not eligible. Tasks which involved assessment of emotional reactivity (Werner et al., 2007), or social decision-making (Grossman et al., 2010) were also not included. One further study was excluded (Fernandez-Duque et al., 2010) because only broad categories of affective attribution were assessed (positive, negative and ambivalent attributions).

Where studies met all four of these criteria, and additionally reported ToM data for an AD control group, these data were also permitted to contribute to the

Please cite this article as: Henry, J. D., et al. A meta-analytic review of theory of mind difficulties in behavioural-variant frontotemporal dementia. *Neuropsychologia* (2014), http://dx.doi.org/10.1016/j.neuropsychologia.2013.12.024