Dementia. Theory of mind

CRISTINA BREDICEAN, CATALIN JIANU, SORIN URSONIU
TIMIŞOARA, ROMÂNIA
The term ‘theory of mind’ was originally proposed by primatologists Premack and Woodruff in a seminal article to suggest that chimpanzees may be capable of inferring mental states of their con-specifics (individuals of the same species) (Premack and Woodruff, 1978).

The concept of a disturbed theory of mind has become important in:

- autistic spectrum disorders (Baron-Cohen et al., 1985)
- ‘endogenous’ psychoses
- heterogeneous disorders affecting frontal lobe functioning
- consumption of psychoactive substances
Introduction

If primate brains, particularly neocortical structures, enlarged over evolutionary time due to selection pressures from the social environment, where exactly is theory of mind located in the human brain?

Comparative neuroanatomy and neurophysiology informs us which brain areas and corresponding functions came under selection pressure in non-human primates to evolve into the neural correlates of theory of mind in modern humans.

Functional brain imaging studies and lesion studies in patients suffering from brain injuries or stroke may help localizing the brain circuits underlying theory of mind.
Anterior cingulate cortex (ACC) 

Error detection, self-consciousness, empathy 

Prefrontal cortex 

Executive functioning, control of social behavior 

Orbito-frontal cortex 

Decision making, ToM 

Temporo-parietal cortex 

Recognition and processing of emotions 

distinction of the self, ToM 

Paracingular cortex 

Amygdala
<table>
<thead>
<tr>
<th>Table 1</th>
<th>Overview of brain imaging studies of theory of mind in chronological order</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author(s) published</td>
<td>Sample (n)</td>
</tr>
<tr>
<td>Goel et al., 1995</td>
<td>9 healthy subjects</td>
</tr>
<tr>
<td>Fletcher et al., 1995</td>
<td>6 healthy subjects</td>
</tr>
<tr>
<td>Happé et al., 1996</td>
<td>5 patients with Asperger syndrome and normal intellectual functioning</td>
</tr>
<tr>
<td>Gallagher et al., 2000</td>
<td>6 healthy subjects</td>
</tr>
<tr>
<td>Bruck et al., 2000</td>
<td>8 healthy subjects</td>
</tr>
<tr>
<td>Russell et al., 2000</td>
<td>5 schizophrenic patients</td>
</tr>
<tr>
<td>McCabe et al., 2001</td>
<td>7 controls</td>
</tr>
<tr>
<td>Vogels et al., 2001</td>
<td>12 healthy subjects</td>
</tr>
<tr>
<td>Calder et al., 2002</td>
<td>8 healthy subjects</td>
</tr>
</tbody>
</table>

(continued on next page)
<table>
<thead>
<tr>
<th>Author(s); published</th>
<th>Sample (n)</th>
<th>Mean age</th>
<th>Sex m/f</th>
<th>Brain imaging technique</th>
<th>ToM method/tasks</th>
<th>Activated brain areas in ToM tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fertil and von Cramon, 2002</td>
<td>9 healthy subjects</td>
<td>24</td>
<td>5/4</td>
<td>fMRI</td>
<td>Presentation of related and unrelated sentence pairs requiring logical explanation or ToM processing.</td>
<td>The frontomedian cortex was activated in coherent and non-coherent trials when ToM instructions were given, and in coherent but not in non-coherent trials when logical/non-ToM instructions were given.</td>
</tr>
<tr>
<td>Brunet et al., 2003</td>
<td>7 patients with schizophrenia</td>
<td>31</td>
<td>7/0</td>
<td>PET [¹⁵O]H₂O</td>
<td>Picture stories involving attribution of intentions by selecting one of three options depicting the logical ending of the story.</td>
<td>In contrast to controls, the schizophrenic patients did not show activation of the right prefrontal cortex during attribution of intentions.</td>
</tr>
<tr>
<td>Calarge et al., 2003</td>
<td>8 controls 13 healthy volunteers</td>
<td>23.3</td>
<td>8/0</td>
<td>PET [¹⁵O]H₂O</td>
<td>Making up a ToM story about a given scenario.</td>
<td>A complex activation pattern was found comprising the medial frontal cortex, superior and inferior frontal regions, the paracingulate gyrus, the cingulate gyrus, the angular gyrus, the anterior pole of the temporal lobe, and the right cerebellum, predominantly on the left.</td>
</tr>
<tr>
<td>Nieminen-von Wendt et al., 2003</td>
<td>8 subjects with Asperger’s syndrome</td>
<td>28.1</td>
<td>8/0</td>
<td>PET [¹⁵O]H₂O</td>
<td>Auditory given ToM stories and physical (control) stories.</td>
<td>During ToM tasks both groups showed increased activation in the occipitotemporal area bilaterally, the right temporal lobe, the thalamus, and the midbrain. The activation in the medial prefrontal area was more intensive and extensive in the control group.</td>
</tr>
<tr>
<td>Saxe and Kanwisher, 2003</td>
<td>8 controls 25 healthy subjects</td>
<td>31.5</td>
<td>8/0 13/12</td>
<td>fMRI</td>
<td>Visually presented stories of false belief, mechanical inference, human action and nonhuman objects.</td>
<td>There was activation of the temporoparietal junction bilaterally only during tasks requiring reasoning about the content of mental states. The left temporoparietal junction was activated during presentation of photographs as well as objects, whereas the right temporoparietal junction showed a trend towards greater activity during presentation of people.</td>
</tr>
<tr>
<td>subgroup of 14 healthy subjects</td>
<td></td>
<td>7/7</td>
<td></td>
<td></td>
<td>Whole body photographs in a range of postures, and inanimate objects.</td>
<td></td>
</tr>
<tr>
<td>Walter et al., 2004</td>
<td>13 healthy subjects</td>
<td>25.15</td>
<td>6/7</td>
<td>fMRI</td>
<td>Comic strips requiring understanding of a person’s intention in a social interaction or a person’s intention in a non-social action.</td>
<td>The anterior paracingulate gyrus was activated by intentional social interactions and in the prospective social intention condition, but not by intentional physical action, whereas in all conditions the anterior cingulate and the superior temporal sulcus were activated.</td>
</tr>
<tr>
<td>Grezes et al., 2004</td>
<td>6 healthy subjects</td>
<td>24–39</td>
<td>4/2</td>
<td>fMRI</td>
<td>A second condition with future intentional social interaction. Presentation of videotapes of the subjects themselves and other actors/participants lifting and carrying a box of different weights. Then subjects had to judge whether the actor had the correct or false expectation of the weight by their nonverbal behaviour.</td>
<td>Contrasting perception of one’s own action with actions of others showed activation in the dorsal premotor cortex, the left frontal operculum, the left intraparietal sulcus and the left cerebellum, which occurred earlier for perception of one’s own action compared with the actions of others.</td>
</tr>
<tr>
<td>Study Authors</td>
<td>Subject Count</td>
<td>Age Range</td>
<td>Session</td>
<td>Imaging</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>---------------</td>
<td>-----------</td>
<td>---------</td>
<td>---------</td>
<td>-------------</td>
<td></td>
</tr>
<tr>
<td>Rilling et al., 2004</td>
<td>19 healthy subjects</td>
<td>28.1</td>
<td>8/11</td>
<td>fMRI</td>
<td>Examination of the main effect of receiving feedback from a human partner or a computer in the Ultimatum Game and Prisoner’s Dilemma Game (PDG). The dorsomedial prefrontal cortex and the rostral anterior cingulate gyrus were activated only in competition with human partners but not computers in the Ultimatum Game. In both tasks only human partners activated the right mid STS, a region spanning the hypothalamus, ventral thalamus and midbrain, and central regions of the hippocampus. In the PDG computer partners also activated the anterior paracingulate cortex, the right STS, thalamus and the left lingual gyrus. There was activation of the medial prefrontal area (approx. BA 9/6/32, 9, 10), the inferior frontal gyrus bilaterally (approx. BA 44, 47), the temporo-parietal regions (approx. BA 21, 22), and of the parahippocampal areas including the amygdala when subjects viewed pretended actions.</td>
<td></td>
</tr>
<tr>
<td>German et al., 2004</td>
<td>16 healthy subjects</td>
<td>18–29</td>
<td>8/8</td>
<td>fMRI</td>
<td>Video clips with actors performing simple everyday actions or pretending to perform a similar set of actions under covert conditions.</td>
<td></td>
</tr>
</tbody>
</table>

BA, Brodmann area; fMRI, functional magnetic resonance imaging; n.m., not mentioned; PET, positron emission tomography; rCBF, regional cerebral blood flow; STS, superior temporal sulcus; ToM, theory of mind.
Testing theory of mind

- The ‘gold standard test’ of comprehending other persons’ minds is to grasp that other can hold false beliefs that are different from one's own (correct) knowledge (Dennett, 1978).

- The classic ‘Sally-and-Anne-Test’ (Wimmer and Perner, 1983) experimentally creates a situation in which a test person has to distinguish his or her own knowledge that an object has been hidden by one character (Anne) in the absence of another person (Sally) from the knowledge of the other characters involved.

- The crucial question is where Sally would look for the object when she returned: The location it was before she left the scene, or the place where Anne had moved it.
Test Sally and Anne

This is Sally. This is Anne.

Sally has a basket. Anne has a box.

Sally has a marble. She puts the marble into her basket.

Sally goes out for a walk.

Anne takes the marble out of the basket and puts it into the box.

Now Sally comes back. She wants to play with her marble.

Where will Sally look for her marble?
More sophisticated cognitive capacities involving a theory of mind include the understanding:

- false belief tasks (e.g. Perner and Wimmer, 1985)
- metaphor irony
- faux pas.

It has been argued that understanding metaphor requires at least first order theory of mind comprehension, whereas irony involves second order theory of mind, because these processes relate to the ability to go beyond the literal meaning of utterances by inferring what the speaker actually might have intended (Happe´, 1994; Langdon et al., 2002b).
False belief task

- What does the person with the blue shirt believe is in the bag? *(false belief)*
  Gift, present, flower, (bug is incorrect)

- What's in the bag? *(reality)*
  Wasp, bee, insect, or bug

- What does the person in blue shirt believe the person in red intends to do? *(2nd order false belief)*
  Give him a gift or present

- What does the person in red assume the person with the blue shirt believes, regarding his (the one in red) intentions? *(3rd order false belief)*
  Give him a gift or present
Faux pas recognition test

Faux pas = breach of etiquette

- Recognition calls for a high level of ToM

Jill had just moved into a new apartment. Jill went shopping and bought some new curtains for her bedroom. When she had just finished decorating the apartment, her best friend, Lisa, came over. Jill gave her a tour of the apartment and asked, “How do you like my bedroom?”

“Those curtains are horrible” Lisa said, “I hope you are going to get some new ones!”

Questions

1. Did Lisa know the curtains were new?
2. Did someone say something she shouldn’t have said?
Theory of mind in frontotemporal dementia and Alzheimer’s disease

- Alzheimer’s disease (AD) and frontotemporal dementia (FTD) are among the most common forms of dementia.

- FTD is primarily characterized by behavioural problems and changes in verbal abilities, social conduct and personality rather than memory problems.

- AD disorder was associated with more severe problems in memory, general cognition and orientation.
In the international consensus criteria for FTD, neuropsychological criteria suggest that FTD is associated with more severe deficits in executive functions, yet relatively preserved memory and visuospatial functions.

Moreover, a number of recent studies showed that memory may be substantially impaired in FTD as well.

Accurate and timely differential diagnosis of AD and FTD is important, as there are significant differences in management of these conditions.
A potential alternative neuropsychological candidate for differentiating between FTD and AD is social cognition.

Such deficits may be early and dominant characteristics of FTD and impaired ability in empathy is among the current behavioural criteria of FTD.

However, assessment of social cognition deficits is not included in current neuropsychological criteria of FTD.
Social cognition ...

- Social perception
- Emotions recognition
  - ToM
  - Attributional style

- Green, Olivier, Crawley, Penn, & Silverstein, 2005; Green et al., 2008; Penn, Addington, & Pinkham, 2006
Additionally, social cognition is likely to be more directly related to interpersonal functioning than cognitive abilities measured by standard neuropsychological batteries.

While research into ToM is relatively new in FTD compared with in autism and schizophrenia, emerging evidence suggests that ToM is also impaired in FTD.

The neuroanatomical profile of FTD primarily includes atrophy in regions that have a role in ToM including ventromedial, lateral temporal and frontoinsular cortices.

Therefore, it is possible that ToM deficits may be more specific to FTD, especially in early phases!!! ... This may have implications for early diagnosis of FTD, and in the differentiation of FTD from AD.
Theory of mind in behavioural-variant frontotemporal dementia and Alzheimer’s disease: a meta-analysis

EMRE BORA, MARK WALTERFANG, DENNIS VELAKOULIS - 2015 -
Current evidence suggests that neurocognitive testing has limited practical benefit in distinguishing frontotemporal dementia (FTD) and Alzheimer’s disease (AD).

In this meta-analysis of 30 studies, theory of mind (ToM) performances of 784 individuals with FTD (n=273) and AD (n=511) were compared with 671 healthy controls.

ToM performances of 227 patients with bvFTD and 229 with AD were also compared in studies matched for general cognition. ToM was impaired in both FTD and AD.
In FTD patients were particularly impaired in advanced tasks such as recognition of faux pas and sarcasm. In AD, ToM deficits were relatively modest. In studies matched for general cognition, ToM was significantly impaired in bvFTD in comparison to AD, especially for faux pas recognition.

ToM dysfunction is a robust and more specific feature of FTD. In contrast, ToM deficits are modest compared with level of general cognitive impairment in AD.

Assessment of ToM can be beneficial for early identification of FTD.
At present ...

- ToM is significantly impaired in both AD and FTD.

- In both disorders longer duration of disease and some severe cognitive deficits were related to ToM deficits.

- In AD, unlike in FTD, ToM deficits were modest in comparison to general cognitive impairment.

- ToM impairment in comparison to controls was especially quite significant in FTD in advanced tasks such as sarcasm and RMET tasks, and especially in faux pas recognition.
In the dementia groups, **faux pas recognition** seems to be the most discriminatory task between AD and FTD.

Some evidence supports this idea, including findings suggesting that impairment in faux pas recognition is related to lesions in the ventromedial frontal cortex.
The faux pas test requires additional social cognitive processes (awareness of social norms) beyond ToM and non-social cognitive abilities.

In FTD, the loss of awareness of social norms, loss of social event knowledge and/or decreased attention to such social norms play a significant role in severe deficits in faux pas recognition.
The pattern of relationship ToM/ general cognition

- In FTD, ToM deficits were at least as severe as general cognitive dysfunction, especially in tasks such as faux pas and sarcasm recognition.

- In contrast, ToM deficits were much less severe than general cognitive dysfunction in AD.
Thank you!!