Hyperintentionality in schizophrenia: An fMRI study

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Abstract

In this fMRI study, we investigated Theory of Mind (ToM) in patients with paranoid schizophrenia. We hypothesized that the network supporting the representation of intentions is dysfunctional in patients with schizophrenia dependent on the type of intention involved. We used a paradigm including a control condition (physical causation) and three intention conditions (private intention, prospective social intention and communicative intentions) differing in the degree of social interaction. Patients showed significantly less activation in three regions typically activated in ToM tasks, i.e. paracingulate cortex and bilateral temporo-parietal junctions. However, this dysfunction was dependent on the type of intention represented, i.e. was present only for social but not for non-social intentions. Moreover, part of the reduced activation was related to the fact that there was no signal drop in these regions for the physical causality condition as usually found in controls. This may be due to the tendency of schizophrenic patients to attribute intentionality to physical objects.

Keywords: Schizophrenia, Theory of Mind, Social interaction, Communication, Intention, fMRI.

Introduction

Theory of Mind (ToM) is the cognitive ability to understand others as intentional agents by inferring and thereby representing their mental states (Frith 2004; Premack & Woodruff, 1978). Functional imaging studies in healthy controls have shown four key regions involved in ToM: The medial prefrontal cortex (MPFC), the posterior cingulate cortex/precuneus and bilateral temporo-parietal regions (TPJ) (Ciaramidaro et al. ,2007; Frith, 2004; Saxe, 2006), which we will call th ToM network. ToM deficits are prominent in autism (Baron-Cohen, 1995) but have also been found to be impaired in patients with schizophrenia (Brune, 2005). Frith (1992) proposed that certain psychotic symptoms associated with schizophrenia reflect a deficit in the ability of mentalizing and claims that this is the result of a failure of patients to monitor their own and others' mental states and behaviour. It has been argued paranoid patients may be characterized by hyperintentionality. Abu-Akel and Bailey (2000) speak about "hyper ToM: Whereas healthy persons are able to reflect on the appropriateness and correctness of these more or less automatic attributions, patients with paranoid schizophrenia might over-attribute significance and intentions to events, person and objects. To date, only few studies have investigated ToM tasks in patients with schizophrenia using cartoons (Brüne et al., 2008; Brunet et al., 2003), and empathy and forgiveness judgments (Lee et al., 2006). These studies yielded inconsistent results with hypo- (Brunet et al., 2003; Lee et al., 2006) as well as hyperactivation (Brüne et al., 2008) of nodes of the ToM network, in particular in the MPFC.

Here we investigate brain activation in a homogeneous group with paranoid schizophrenia for non-social and social ToM tasks with a validated experimental setting (Walter et al., 2004; Ciaramidaro et al., 2007) using three different types of intention (private intentions, prospective social intention, communicative intentions) and a physical causation control condition. We hypothesize a dysfunction in the mentalizing network in terms of reduced brain activations in the intentional conditions, in particular for communicative intentions (CInt), because the schizophrenic patients' attitude of "over-attributing" intentions seems to be related to violations of pragmatic rules in their use of language and incorrect inferences of communicative intentions (Brüne, 2005).

Methods

Subjects

We studied 12 right-handed patients with paranoid schizophrenia according to ICD-10 (F 20.0)/DSM-IV (6 females, mean age 29.41, PANNS total 73.75) recruited from among the inpatients treated at the Department of Psychiatry at the University of Ulm, as well as a matched control group with mean age 24.75 years (SD 2.63). The University of Ulm's ethics committee approved the study.

Experimental design

In our task, participants were asked to look at short comic strips and then choose a picture that showed the only logical story ending. Comic strips pertained to the following experimental categories: The first category were intentions of single agent acting in isolation, i.e. 'private intentions' (**PInt**), for example, changing a broken bulb in order to read a book. The second category were intentions of a single agent acting in isolation (like in the PInt condition) which however, intends to socially interact (prospected social interaction, **PSInt**), for example a single person preparing a romantic dinner. A third category were 'communicative intentions' (**CInt**), i.e. intentions involving two persons interacting, for example a person asking for a glass of water to another person. The CInt condition does not require a second order ToM. As a control condition we used physical stories depicting non intentional physical causality (**Ph-C**), for example, a ball blown by a gust of wind knocks over and breaks several bottles. We presented comic strips consisting of a sequence of three pictures (the story-phase); each picture was displayed for 3 seconds. The story phase was followed by a choice-phase, during which three possible solutions were displayed simultaneously for 7 seconds. Thus, one trial (one comic strip) lasted 16 sec (story-phase plus choice-phase). Participants indicated their choice by pressing one of three buttons as quickly as possible. Only one picture represented the correct answer. The two uncorrected pictures were constructed according to the following principle: The first foil picture showed a possible, but illogical ending. The second one included the objects of the last scene of the story-phase rearranged physically without containing a real action. Eleven comic strips were presented for each of the four conditions, summing up to a total of 44 trials presented in pseudo randomized order. The experimental protocol was administered in two sessions of 22 trials each. Before scanning each participant received training During scanning, participants wore luminescent crystal display glasses. Stimuli were presented with Presentation software (Neurobehavioral Systems).

Behavioral Data Analysis

Participant reaction times and response accuracy were measured during scanning. Data were analyzed in a one-way ANOVA with subsequent comparisons between means, using Bonferroni's post hoc test.

fMRI data acquisition and analysis

fMRI data were acquired using a 1.5 Tesla Siemens Magnetom Symphony whole-body MRI System equipped with a head volume coil. T2* weighted functional MR images were obtained using echo-planar imaging in an axial orientation. Image size was 64 x 64 pixels, with a field of view of 192 mms. One volume covering the whole brain consisted of 25 slices with 4mm slices thickness and a 1mm gap. Time of repetition (TR) was 2.250 s, echo time (TE) was 40 ms. One session contained 257 volumes. Data pre-processing and statistical analysis were conducted with SPM 2 (Statistical Parametric Mapping, Wellcome Institute of Cognitive Neurology, London, UK) and MATLAB 6.3 (MathWorks, Natick, Massachusetts, USA) using standardised procedures (Friston et al., 1995).

In a first level analysis each subject was analysed separately. Regressors were defined for story-phase and choice-phase for each of the four conditions separately as box cars convolved with the canonical hemodynamic response function implemented in SPM2. Realignment parameters were included in the model. Contrast images for each condition (Ph-C, PInt, PSInt and CInt) were calculated by using the regressors for story and choice phases together. To account for interindividual variance and in order to generalise inferences (Holmes & Friston, 1998), we conducted a second level analysis using an ANOVA and contrasting each of the intentional conditions (PInt; PSInt and CInt) with the control condition (Ph-C). Group comparisons were also computed using an ANOVA using the same contrasts utilised in the within-group comparisons. Results are from second level random effect analysis (ANOVA) and we chose an uncorrected threshold of $p < 0.001$ at the voxel level, corrected for extent ($p < 0.05$) at the cluster level (Forman et al., 1995).

Results

Behavioral results

Analysis of reaction times in ms (for correct answers only) showed a main effect of group: Patients were slower than the control group for $F(1,22)=9.105$, $P = 0.006$ but there was no interaction between reaction time and group ($F(3,66)=0.593$, $p = 0.62$). Similar results were obtained for response accuracy: patients made more errors than the control group ($F(1,22)=37.8$, $p < 0.0001$) but there was no interaction between condition and group ($F(3,66)=0.39$, p

= 0.75).. T-tests for reaction time revealed the following results: For Ph-C p= 0.026, for PInt p= 0.013, for PSInt p= 0, 011 and CInt p= 0.002; T-tests for accuracy for all four comparisons p>0.001.

Neuroimaging results

ANOVA between groups comparing contrasts of interest in controls and patients revealed significantly elevated activations only in the control group compared to the patient group and not vice versa. The contrast PInt versus Ph-C reveals no differences between the two groups in nodes of the ToM network. In the contrast PSInt versus Ph-C the right TPJ and MPFC were activated significantly more in the control group and the contrast CInt versus Ph-C indicates significant group differences in the right and left TPJ and the MPFC (Figure1).

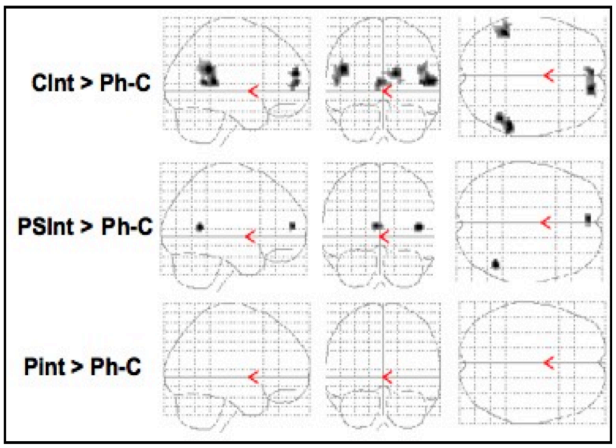

Figure 1: Regions in which healthy controls showed relatively more cerebral activation compared with paranoid patients for PInt, PSInt, CInt versus control condition (Ph-C). 2nd level ANOVA, p<0.001 uncorrected, p<0.05 at the cluster level.

A clearer picture emerges if the mean activation sizes per condition and group are plotted (compare Figure 2): Whereas the control group also exhibited parametric activation in this region, the patient group showed positive beta parameters for the Ph-C and for the CInt condition and negative beta parameters that were similar for the PInt and PSInt conditions.

Discussion

Behavioural impairments

The patient group showed lower accuracy and increased reaction times compared to the control group. However, reduced performance was observed in all four conditions, i.e. also the control condition (Ph-C). Brunet et al. (2003) using a ToM task similar to ours, reported similar results, i.e. reduced performance in ToM as well as the control task. We assume these findings as a consequence of the patients exhibiting "hyper-ToM"leading these patients to attribute intentions to objects, treating things like persons.

Impairment of neural mechanisms supporting ToM

The present study aimed at investigating the dysfunction of the ToM network in paranoid schizophrenia and its modulation by different intention types: PInt, PSInt and CInt. Confirming our hypothesis, we found a dysfunction of the ToM network.

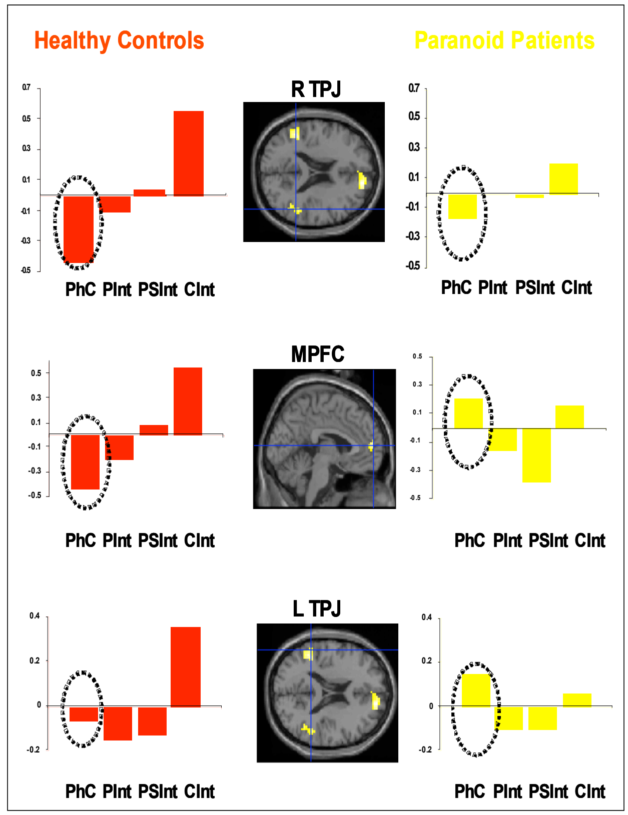

Figure 2: Mean activation effects of the contrast CInt vs Ph-C for right TPJ, MPFC and left TPJ. The activation effects were extracted from the second level between-group ANOVA, P < 0.001 uncorrected, P < 0.05 at the cluster level. Red: Healthy group; Yellow: Paranoid patients. Dashed circle indicate the beta parameters for the control condition (Ph-C).

Our results are consistent with findings by Brunet et al. (2003) using a similar cartoon paradigm who also found less activation in the right MPFC in patients with schizophrenia. However, as we will discuss below, the findings of Brunet et al. (2003) mixed the types of intentions which might explain why they could not demonstrate hypo-activation of the TPJ. Similar findings have been described by Marjoram et al. (2006) comparing high risk subjects with and without psychotic symptoms. In a recent study by Brüne et al. (2008) however, increased activation of dorsomedial areas, left TPJ and right temporal cortex were found in patients with schizophrenia compared to controls. Furthermore, the task used by these authors did not show a robust activation of the ToM network in healthy controls, who showed no activation of the MPFC, perhaps due to the fact that activation and control task were quite similar. One strength of our paradigm is that it allows to investigate group differences for different types of intentions. For the PInt condition, representing the most simple ToM condition, we found no group differences. Instead, during PSInt, significant group differences in the right TPJ and the MPFC were revealed. Although both intentions (PInt and PSInt) share a common element, namely a single agent acting in isolation, only PSInt requires the representation of a social goal. Also in CInt, there was an additional group difference in activation in the left TPJ (together with the right TPJ and the MPFC). How can we understand these groups differences which are restricted to social intentions only? Our results show that as soon as social interaction is involved (present or foreseen) neural differences in activation become apparent. This is true for the most basic structure of the ToM network, namely the right TPJ (Saxe & Wexler, 2005). Significant group differences are also found in the MPFC. It has been argued that the MPFC serves the purpose of decoupling mental states from their environment (Brüne, 2005; Brunet-Gouet & Decety, 2006). This function helps subjects to distinguish between what is happening in the outer world and what in the inner world. Patients with schizophrenia show an aberrant pattern of activation for social intentions, probably because they are not able of decoupling and have problems distinguishing between intentions of others interacting and their own, resulting in misattributions. In the CInt condition group differences were most pronounced and incorporated additionally the left TPJ. The left TPJ has been shown to be specifically activated for communicative intentions (Ciaramidaro et al., 2007).

Interestingly, our data reveal further information related to the control condition (Ph-C). Looking at the beta parameters in Figure 2, it is obvious that the lack of activation in the MPFC anf TPJ for the contrast CInt vs. Ph-C is not only due to decreased activation in these regions in the CInt condition, but also to relatively increased beta values in the Ph-C condition. In accordance with the above mentioned hypothesis that paranoid schizophrenic patients may have a hyperactive intention detector, we can explain our results as follows: Paranoid patients do not deactivate their intention detector when they are solving stories involving physical causality but these patients are always in an 'online' modus of ToM. This would also be the case in contexts without intentional agents, where no ToM is required. Blakemore et al. (2003) reported that patients with delusions of persecution attributed intentional behaviour to moving shapes in conditions where controls saw no intentionality. These authors propose that patients with schizophrenia perceive agency where others see none. The same process took place when our patient group observed Ph-C stories. An exaggerated sense of agency seems to characterize patients with delusions of persecution, and this tendency to perceive agency where there is none may be a more general feature of schizophrenia (Frith, 2005).

We provide evidence that the dysfunction in the intentional network is partially mediated by an intention detector which became hyper-active in the paranoid interpretation of the physical world. Hence, we agree with the idea of "hyper ToM" as proposed by Abu-Akel and Bailey (2000): "An attitude to associate with quantitative overgeneration of hypotheses or overattribution of mental states" also when ToM is not demanded.

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