The neural substrates of diminished humor comprehension in schizophrenia and its relationship with psychopathology

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Patients with schizophrenia commonly revealed difficulties in understanding humor. Previous research suggested links between impaired humor comprehension, psychopathology symptoms and cognitive deficits. In this study, we investigated the associations between neural substrates of humor processing and psychopathology and cognition in schizophrenia. We assessed 25 schizophrenia outpatients in an functional magnetic resonance imaging (fMRI) procedure and 40 in an electroencephalography (EEG) procedure. A punchline-based humor comprehension task was used in which outpatients rated stories by their comprehensibility and funniness. The symptom severity and cognition were correlated with activation within the humor processing network using fMRI and effective connectivity using an EEG-directed transfer function (DTF) method. More severe positive and disorganization symptoms were associated with impaired humor comprehension and with altered temporo-parietal effective connectivity during humor processing. More severe excitement and emotional reactivity symptoms were associated with increased activation in the bilateral frontal and temporo-parietal regions. Moreover, schizophrenia outpatients with better cognitive functioning were more accurate in humor comprehension that was associated with increased fronto-temporo-parietal activation and effective connectivity. We found the intensity of humor processing (fMRI) in schizophrenia is related to the level of cognitive abilities and the severity of schizophrenia psychopathology that is also reflected in altered effective connectivity (EEG-DTF) in the humor processing network.

Key words: electroencephalography, neuroimaging, psychopathology, schizophrenia, figurative language

INTRODUCTION

Disturbance in humor, as a part of a figurative language deficit, is considered a key feature of schizophrenia and has been widely studied on the behavioral level (Corcoran et al., 1997; Marjoram et al., 2005a, 2005b; Bozikas et al., 2007; Tsoi et al., 2008; Adamczyk et al., 2017). It is believed that the humor comprehension difficulties stem from problems in semantic cognition, e.g., set shifting of semantic meaning in a given linguistic context in which patients with schizophrenia tend to lean towards literal instead of figurative meaning (Kuperberg et al., 1998; Kircher et al., 2007; Polimeni et al., 2010).

Humor, apart from metaphor processing, is perhaps the most studied component of figurative speech in the healthy population. Humor comprehension has been studied in various modalities, including funny
cartoons, comedic videos and written jokes (Vrticka et al., 2013), all of which share the same nature of a surprise ending that elicits a humorous response. This was described theoretically with the step-by-step model, as one needs to detect the incongruency of semantic meaning, resolve the surprising incongruity and elaborate on the content of a joke (Suls, 1972; Wyer and Collins, 1992; Chan et al., 2012, 2013).

To date, multiple brain regions in the humor-related network have been identified, including the medial prefrontal cortex (mPFC), posterior cingulate cortex (PCC), precuneus, superior temporal gyrus (STG), superior temporal sulcus (STS), anterior cingulate cortex (ACC) and the temporoparietal junction (TPJ) (Vrticka et al., 2013). Recent data indicate that patients with schizophrenia show abnormalities during humor comprehension that are reflected in left hemisphere hypofrontality (Adamczyk et al., 2017, 2018; Berger et al., 2018), along with suppression of right temporoparietal cortex activity (Adamczyk et al., 2017, 2018), and abnormal lateralization in directionality of effective connectivity (Adamczyk et al., 2019).

Despite the above findings regarding humor-processing disturbances and their neural substrates in schizophrenia, the relationship between brain activity and psychopathology symptoms or cognitive deficits remains understudied. Previous data indicate that schizophrenia individuals find jokes more difficult to understand when mentalizing abilities (Theory of Mind) are involved (Corcoran et al., 1997), and the humor comprehension is more impaired in patients with more severe positive symptoms, such as delusions (Corcoran et al., 1997; Tsoi et al., 2008). However, the contradictory findings indicate no relationship between humor processing or any psychopathology symptoms (Polimeni and Reiss, 2006). On the other hand, the training of the humor competences (Cai et al., 2014) or exposure to humorous videos (Gelkopf et al., 2013) have been shown to decrease negative symptoms in patients with schizophrenia. Finally, there are some indications that psychopathological symptoms, e.g., disorganization, might be linked with neurocognition (Ventura et al., 2013; Minor and Lysaker, 2014). Cognitive deficits constitute one of the major features of schizophrenia (Schaef er et al., 2013) and the research in context of cognitive processing of humor is scarce. In particular, it has been found that humor comprehension is retained in schizophrenia patients with higher general intellectual and executive functioning (Polimeni et al., 2010) and is also more related to underlying cognitive deficits than to positive or negative symptoms (Bozikas et al., 2007).

Summarizing, even the neural substrate of impaired humor processing in schizophrenia was already pre-determined by pieces of neuroimaging evidence, the findings regarding its relationship with the severity of specific psychopathology symptoms or cognitive deficits remain inconsistent and seemingly far away to be fully understood. In this study, we address this issue by integrating multiple neuroimaging methods (fMRI and EEG-directed transfer function; EEG-DTF) and implementing the three-stage model of humor processing that was applied in our previous studies (Adamczyk et al., 2017, 2019) to reanalyze data concerning psychopathology. We did this in two consecutive steps. In the first step, we selected the regions of interest forming a figurative language network based on our previous findings (Adamczyk et al., 2017). In the second exploratory step, we investigated the possible associations of the activity and connectivity in these regions with psychopathology and cognition.

METHODS

Subjects

In this study, we recruited 40 schizophrenia outpatients through a local outpatient clinic, which sample was examined in our previous studies published elsewhere (Adamczyk et al., 2017, 2018, 2019). All of the 40 participants went through the EEG procedure, and 25 of them also underwent MRI scanning. The symptom severity we assessed using the positive and negative syndrome scale (PANSS) (Kay et al., 1987) with the 30-item 5-factor model (dimensions including positive, negative, disorganization, excitement and emotional distress symptoms) described by van der Gaag et al. (2006). The cognitive abilities were assessed using the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005), a brief examination that we selected due to extensive neuroimaging part which performs well in detecting cognitive deficit in schizophrenia (Fisekovic et al., 2012; Yang et al., 2018). All procedures were approved by the Bioethical Committee at Jagiellonian University in Krakow, Poland, and were designed in accordance with the ethical standards of the World Medical Association Declaration of Helsinki (2013). Every participant gave informed consent to participate in the experimental procedures. Every patient was in a stable psychopathological condition and was receiving antipsychotic medication for several weeks before the experiment. All the participants were native Polish speakers and right-handed. Exclusion criteria were any history of head injuries, seizures, substance dependence or any serious current somatic illnesses that could affect brain integrity. Demographic and clinical data are presented in Table I.
Experimental procedure

The punchline-based humor comprehension task contains text stories with different endings in three conditions: funny (FUN), neutral (NEU) and absurd (ABS) punchlines. During the experimental task, each participant was presented with 60 text-based stories in a randomized order, with each of the three endings having 20 items (FUN, NEU, ABS). First, subjects rated whether the punchline fitted the story (yes/no comprehensibility rating) and then assessed the funniness of the story on a 9-point scale (funniness rating). The EEG and fMRI versions used the same design with two different sets of stories. Both sessions were conducted within one-week period. The experimental design, stimuli and procedures of the punchline-based humor-comprehension tasks were described in detail in our previous fMRI and EEG reports on humor processing in schizophrenia (Adamczyk et al., 2017, 2019).

During the experiment in an EEG laboratory, subjects were presented stories on a computer screen. They responded by pressing keys on a standard keyboard. During the experimental MRI session, the stories were displayed on an MRI-compatible screen and responses were collected using fibre-optic response button grips (Nordic Neuro Lab, Bergen, Norway). Subjective responses of comprehensibility and funniness ratings and subjects’ reaction times were recorded for each stimulus with no time limit for the answer.

MRI and EEG data acquisition

MRI data were acquired using a 3T scanner (Magnetom Skyra, Siemens) with 32-channel head coil at Malopolska Centre of Biotechnology. Functional data were collected using EPI sequence with following parameters: 37 axial slices (TR=2000 ms; TE=27 ms; FOV 192 × 192 mm²; flip angle=90°; 3 mm isotropic voxel). Images were taken in an interleaved, ascending fashion. The B0 inhomogeneity field map was acquired with a dual-echo gradient sequence matched spatially with the fMRI scans. Additionally, anatomical images were acquired with standard T1 MPRAGE sequence (sagittal slices; 1 × 1 × 1.1 mm3 voxel size; TR=2300 ms, TE=2.98 ms).

The EEG was recorded with a Biosemi Active Two amplifier, and 32 active electrodes on a standard 10–20 headcap, with four additional sensors for recording oculomotor activity and two more electrodes for offline linked mastoid reference. Sample rate was set to 256 Hz.

Behavioral data analysis

Behavioral data were analyzed as a total sum from subjects who completed both MRI and EEG procedures (n=25). Comprehensibility was computed as a sum of ratings, while funniness was averaged from ratings of

Table I. Demographic and clinical data.

|                      | EEG (n=40) | fMRI (n=25) |
|----------------------|------------|-------------|
|                      | Mean      | SD         | Mean      | SD         |
| Age                  | 42.60     | 10.12      | 42.36     | 9.99       |
| Education (years)    | 14.80     | 2.90       | 14.36     | 2.68       |
| Illness duration (years) | 19.40   | 10.12      | 18.72     | 8.92       |
| Number of psychotic episodes | 9.40   | 7.40       | 10.60     | 8.49       |
| Number of hospitalizations | 7.73   | 5.13       | 7.56      | 5.24       |
| Chlorpromazine equivalents (mg/day) | 440   | 299        | 505       | 338        |
| PANSS Total          | 57.40     | 18.34      | 57.24     | 16.31      |
| PANSS Positive       | 10.68     | 4.81       | 10.80     | 4.73       |
| PANSS Negative       | 15.80     | 7.23       | 15.52     | 5.71       |
| PANSS Disorganization | 8.78    | 4.09       | 9.16      | 4.33       |
| PANSS Excitement     | 6.08      | 2.38       | 6.04      | 2.47       |
| PANSS Emotionality   | 8.35      | 3.03       | 8.20      | 2.75       |
| MoCA                 | 23.90     | 3.23       | 24.16     | 3.14       |

SD, standard deviation; PANSS, positive and negative syndrome scale; MoCA, Montreal Cognitive Assessment.
a 9-point scale for each of the three conditions (FUN, ABS, NEU). To investigate the relationship between humor processing and psychopathology, we used Spearman’s non-parametric partial correlations using age (years), sex, illness duration (years) and antipsychotic medication (as chlorpromazine equivalents in mg/day) as covariates. The results are reported at P<0.05 with false discovery rate (FDR) correction for multiple comparisons (Benjamini and Hochberg, 1995) and due to the exploratory nature of the study also uncorrected P<0.05.

**fMRI data preprocessing and analysis**

We performed the data processing and analysis in SPM12 software (Statistical Parametric Mapping, Wellcome Department of Cognitive Neurology, London, UK). The images were unwarped using a field map correction, motion correction, realigned with a six-parameter rigid body transformation (motion correction) and co-registered to the anatomical reference image. Images were then segmented into separate tissues and normalized to MNI space with 3 mm isotropic voxels using a 12-parameter affine transformation, and spatial smoothing with 8 mm Gaussian kernel. We used the ART toolbox to detect and reject scans with excessive movements relative to the previous scan with the following threshold parameters: global intensity 3 z, linear movements (x, y, z) 1 mm, and rotations (p, r, y) 0.02°. We removed five subjects from further analysis who had scan rejection rates over 20%

For within-group contrasts, we applied the general linear model (GLM) with standard and extended motion parameters. Three separate models were applied. The first included setup, punchline (with three levels: FUN, ABS, NEU) and the response period. Three main within-group contrasts were provided separately in both experiments: incongruity detection (ABS vs. NEU); incongruity resolution and elaboration (FUN vs. ABS); complete humor processing (FUN vs. NEU) (Adamczyk et al., 2017; 2019). To investigate the neural activation during humor processing represented by the aforementioned contrasts and psychopathology, we used the GLM model with 6 main regressors (5 PANSS subscales: positive, negative, disorganization, excitement, emotional responsibility; and MoCA) and 4 covariates of no interest (age, sex, illness duration and chlorpromazine equivalent). We calculated the parametric voxel-wise Pseudo-t test with variance smoothed with full width at half maximum 6 x 6 x 6 mm and 10,000 permutations using a mask of selected areas of the Neuromorphometric atlas based on a combination of regions of interest that were previously described in our other paper (Adamczyk et al., 2017). The regions of interest include rectus g., orbital g., frontal superior g., frontal middle g., frontal inferior opercular g., frontal inferior orbital g., frontal inferior triangular g., temporal pole, inferior temporal g., middle temporal g., superior temporal g., transverse temporal g. Heschl’s g., angular g., supramarginal g., precuneus g., anterior cingulate cortex, middle cingulate cortex, posterior cingulate cortex. The results are reported as a local maximum threshold at k≥10 voxels and uncorrected P<0.001.

**EEG-DTF data preprocessing and analysis**

The EEG-DTF preprocessing was conducted using the EEGLab toolbox and included filtering (3 to 45 Hz with zero phase-shift filters), downsampling to 128 Hz, a custom procedure for removing blink contaminations by subtracting individually fitted blink curves (Wyczansky et al., 2018), and epoching in a time window of 0 to 1 s relative to punchline onset. Segments with artefacts exceeding the 100 μV threshold on any of the electrodes were rejected. The autoregression model order was set to 8 based on the Akaike information criterion. The estimation of effective connectivity measures was obtained by calculating non-normalized DTF values for all pairs of electrodes between all predefined ROIs and in the beta band (14 Hz–25 Hz) using the Multar toolbox (Faculty of Physics, University of Warsaw). The distributions of the obtained DTF values were then manually checked to identify possible extremes. Those which were defined as falling below Q1-1.5*IQR or above Q3+1.5*IQR, where Q is quartile and IQR is interquartile range were rejected (Ligeza et al., 2016). The linear mixed-model statistics from the lme4 R package (Bates et al., 2015) were used to test the effects of symptoms (i.e., five PANSS subscales and MoCA) on connectivity measures. Possible interactions with conditions were included, and we controlled for measures (covariates) that could affect the effective connectivity (sex, age, illness duration, chlorpromazine equivalent). Therefore, a separate model was designed for each PANSS subscale and MoCA. Data were visualized with Trans3D (Blinowski et al., 2014). The alpha level was set at P=0.001.

**RESULTS**

**Behavioral associations with clinical variables**

Initially, after applying FDR correction for multiple comparisons, we found that more severe positive symptoms were associated with ratings of the absurd...
punchlines as comprehensible \((r=0.77, P=0.010)\); and that more severe disorganization symptoms were associated with ratings of absurd punchlines as funny \((r=0.69, P=0.039)\).

Subsequently, we explored further associations without correction for multiple comparisons. First, we found that more severe disorganization symptoms were associated with ratings of the absurd punchlines as comprehensible \((r=-0.54, P=0.024)\); and that more severe disorganization symptoms were associated with the ratings of neutral \((r=0.54, P=0.027)\) punchlines as funny. Second, we found that better cognitive functioning (MoCA total score) was positively associated with the correct rating of absurd punchlines as nonsensical and funny punchlines as comprehensible. Third, we found that more severe excitement symptoms were associated with slower reaction times when assessing both the comprehensibility and funniness of the stories. Detailed results are presented in Table II. Interestingly, we found that longer duration of illness was associated with incorrect rating of absurd punchlines as comprehensible \((r=-0.62, P=0.003)\) and funny \((r=0.71, P<0.001)\).

**BOLD signal associations with clinical variables**

We found a positive association between psychopathology variables and BOLD activations during incongruity resolution and elaboration (FUN-ABS) and complete humor processing (FUN-NEU) contrasts (Table III). Specifically, for resolution and elaboration we found an association between excitement symptoms and activation in the left superior frontal gyrus (SFG), between emotional reactivity and activation in the bilateral SFG, and between MoCA score and activation in the left STG. For complete humor processing, we found an association between excitement symptoms and activation in the bilateral SFG, left IFG, left pSTG, right posterior middle temporal gyrus (pMTG) and right TPJ.

### Table II. Correlations of ratings and reaction times during humor comprehension with psychopathological symptoms and cognition.

| Condition | Positive and negative syndrome scale | Cognition |
|-----------|--------------------------------------|-----------|
|           | Positive | Negative | Disorganization | Excitement | Emotional responsivity | MoCA |
| Ratings   |          |          |                  |            |                       |       |
| Absurd    | -0.77**  | -0.08    | -0.54*           | 0.08       | -0.19                 | 0.55* |
| Neutral   | -0.32    | 0.16     | -0.13            | 0.02       | 0.03                  | 0.41  |
| Funny     | -0.36    | -0.03    | -0.20            | 0.05       | 0.20                  | 0.49* |
| Funniness |          |          |                  |            |                       |       |
| Absurd    | 0.39     | 0.03     | 0.69**           | 0.11       | -0.05                 | -0.48 |
| Neutral   | 0.40     | 0.10     | 0.54*            | 0.17       | -0.17                 | -0.48 |
| Funny     | 0.10     | -0.16    | -0.18            | 0.30       | -0.19                 | -0.31 |
| Reaction times |          |          |                  |            |                       |       |
| Comprehensibility |          |          |                  |            |                       |       |
| Absurd    | -0.09    | 0.26     | 0.30             | 0.53*      | 0.04                  | -0.05 |
| Neutral   | 0.00     | 0.31     | 0.17             | 0.72**     | 0.13                  | -0.02 |
| Funny     | -0.11    | 0.03     | 0.16             | 0.59*      | -0.14                 | -0.18 |
| Funniness |          |          |                  |            |                       |       |
| Absurd    | -0.01    | 0.19     | -0.25            | 0.39       | 0.14                  | 0.05  |
| Neutral   | 0.00     | 0.13     | -0.31            | 0.54*      | 0.01                  | -0.03 |
| Funny     | 0.05     | -0.11    | -0.38            | 0.53*      | 0.11                  | -0.04 |

Controlling for age, sex, illness duration and antipsychotic medication. Significant correlations are marked with \(P<0.05\) uncorrected (*) and FDR corrected (**).
between emotional reactivity and activation in the left SFG, left MFG and left inferior parietal lobule (IPL) with supramarginal gyrus, and between MoCA score and activation in the left anterior STG with temporal pole, posterior STG, and right pMTG.

**EEG-DTF effective connectivity associations with clinical variables**

We found significant associations between psychopathology and effective connectivity during incongruity detection and complete humor processing (Fig. 1 and Table IV). For incongruity detection, positive symptoms were associated with decreased connectivity from left IFG to left dLPFC and from right dLPFC to left IPL; disorganization symptoms were associated with increased connectivity from left posterior temporal lobe (pTL) to right dLPFC; MoCA score was associated with decreased connectivity from left anterior temporal lobe (aTL) to right pTL.

**DISCUSSION**

To the best of our knowledge, the present study for the first time investigates neural correlates of the relationship between humor comprehension and psychopathology symptoms and cognitive impairment in schizophrenia. At the behavioral level, we found that patients with more severe positive and disorganized symptoms found absurd and literal punchlines as com-
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prehensible and funny. Concerning neural substrates of humor processing disturbances, we found that schizophrenia symptoms are associated with increased activation and specific effective connectivity in bilateral frontal and temporo-parietal regions during processing of humor stimuli. Moreover, we found that better cognitive functioning was associated with more successful humor comprehension, which was reflected in weaker fronto-temporo-parietal activation and effective connectivity.

First, on the behavioral level, more severe symptoms were associated with more errors. In particular, patients with more severe positive and disorganized symptoms tended to view absurd punchlines as more comprehensible, and those with more severe disorganized symptoms also tended to find absurd and neutral punchlines funny more often. While some studies found no relationship between psychopathological symptoms and humor appreciation (Marjoram et al., 2005b; Bozikas et al., 2007), others demonstrated humor processing in schizophrenia to be associated to delusions (Tsoi et al., 2008), or disorganization and negative symptoms (Corcoran et al., 1997). Bozikas et al. (2007) suggests that this could be due to different approaches to measurement of symptoms that use either standard symptom scales, e.g., PANSS (Marjoram et al., 2005b; Bozikas et al., 2007), or certain schizophrenia subtypes and current clinical symptoms (Corcoran et al., 1997). Therefore, we assume that these discrepancies could be a result of not only the different approaches to measurement of symptoms but also to inconsistent measurement of humor processing. In addition, the lack of reported association between humor processing and specific symptoms might be in part attributed to false negative results, as it is possible that some studies were simply not able to detect the supposed relationship. In our study, the experimental design allowed us to detect specific types of errors. Thus,

| Direction from source to receiver (pairs of electrodes) | PANSS sub-scale | beta   | P     |
|--------------------------------------------------------|-----------------|--------|-------|
| Incongruity detection (ABS-NEU)                         |                 |        |       |
| L TPJ to L IPL (cp5→p3)                               | PANSS positive | -0.3297| 0.0007|
| L IFG to L dIPFC (f7→f3)                              | PANSS disorganization | 0.4284| 0.0001|
| Complete humour processing (FUN-NEU)                   |                 |        |       |
| L IFG to L dIPFC (f7→f3)                              | PANSS disorganization | 0.4122| 0.0002|
| P dIPFC to L IPL (f4→p3)                              | PANSS disorganization | 0.3624| 0.0009|
| L pTL to P dIPFC (p7→f4)                              | PANSS disorganization | -0.3658| 0.0007|
| L aTL to P pTL (t7→p8)                                | MoCA            | -0.3147| 0.0009|

List of regions of interest (ROIs) and directions of electrode pairs (source → receiver) and their correlations with psychopathology symptoms for incongruity detection (ABS-NEU) and complete humour processing (FUN-NEU) contrasts. Statistics for contrast presented as within-group standardized beta coefficients in the appropriate correlation. L, left; R, right; PANSS, positive and negative syndrome scale; MoCA, Montreal Cognitive Assessment; dIPFC, dorsolateral prefrontal cortex; IFG, inferior frontal gyrus; aTL, anterior temporal lobe; pTL, posterior temporal lobe; TPJ, temporo-parietal junction; IPL, inferior parietal lobule.

Fig. 1. Humor comprehension and psychopathology symptoms in schizophrenia. Effective connectivity map. L, left; R, right; PANSS, positive and negative symptoms scale; MoCA, Montreal Cognitive Assessment; vmPFC, ventromedial prefrontal cortex; dmPFC, dorsomedial prefrontal cortex; dIPFC, dorsolateral prefrontal cortex; IFG, inferior frontal gyrus; aTL, anterior temporal lobe; pTL, posterior temporal lobe; TPJ, temporo-parietal junction; IPL, inferior parietal lobule; Prec, precuneus.
the currently observed tendency in outpatients with more severe disorganized or positive symptoms (e.g., rating absurd punchline as comprehensible, or literal meaning as funny), might be considered as a phenomenon that could not be captured by previous studies on humor processing in schizophrenia.

Furthermore, patients with more severe positive symptoms had increased left-hemisphere connectivity during incongruity detection in the temporo-parietal cortex (pTL to IPL), while more severe disorganization symptoms were associated with increased left-frontal connectivity (IFG to dlPFC). This latter association (left IFG to left dlPFC) remained visible during complete humor processing, in addition to increased connectivity from the right dlPFC to the left IPL and decreased connectivity from the left pTL to the right dlPFC. Note that disorganization symptoms are linked with impaired frontal and parietal activation (Quintana et al., 2003; MacDonald et al., 2005), decreased lateralization of fronto-parietal network (Rotarska-Jagiela et al., 2010) and decreased grey matter density in these areas (Palaniyappan et al., 2015). Rotarska-Jagiela et al. (2010) suggest that recruitment of abnormally lateralized areas for semantic processing might contribute to disorganization symptoms. We can suppose that changes in effective connectivity within the left hemisphere may serve as a neural substrate of positive and disorganization symptoms’ effect on humor processing.

In the case of fMRI, the stronger association between symptoms and humor comprehension was related to the stronger BOLD signal in the bilateral frontal and temporo-parietal regions. Specifically, for the incongruity resolution and elaboration contrast, we found an association between both excitement and emotional reactivity with activation in the left SFG. Compared to controls, this region has previously been found to be hyperactivated in schizophrenia during comprehension of humorous stimuli (Adamczyk et al., 2017). For complete humor processing, we found a relationship between excitement and widespread activation in the bilateral SFG, left IFG, left pSTG, right pMTG and right TPJ and between emotional reactivity and bilateral SFG activation. It is noteworthy that on a behavioral level no relationship was found between emotional reactivity or excitement and ratings of comprehensibility and funnyess. However, more severe excitement symptoms were associated with delayed responses, indicating that humor processing is perhaps more demanding for schizophrenia patients. Besides, more pronounced engagement of the frontal and temporo-parietal regions without differences in comprehensibility or funnyess ratings could signify a compensatory mechanism.

Lastly, our results support the previous findings that humor comprehension is retained in patients with higher cognitive functioning (Bozikas et al., 2007; Tsoi et al., 2008; Polimeni et al., 2010). This relationship remains even when anxiety or depression is controlled for (Polimeni et al., 2010) and is most pronounced for executive functioning (Tsoi et al., 2008; Polimeni et al., 2010). These findings indicate that some aspects of humor comprehension in schizophrenia depend on underlying cognitive functioning, and its impairment is a stable trait in schizophrenia (Bora and Murray, 2014).

Regarding the fMRI results, we found a relationship between cognition and BOLD activation during humor processing. Specifically, for the incongruity resolution and elaboration contrast, we found an association between MoCA score and engagement of the left STG. For complete humor processing, we found an association between MoCA score and activation in the left anterior STG (with temporal pole), posterior STG, and right posterior MTG. The left superior temporal cortex plays a crucial role in semantic processing, speech perception and production and has been associated with grey matter volume reduction during the transition into psychosis, or the early phase of schizophrenia. The activation of temporal regions that are associated with cognition during humor processing would suggest the role of semantic information abnormalities. Interestingly, the results of Bozikas (2007) suggest that phonemic but not semantic fluency impairment is associated with attenuated humor comprehension in schizophrenia, which implies frontal lobe involvement. However, our neurocognitive assessment did not allow such discrimination, therefore future research should address this problem further. Nevertheless, our results suggest that cognition plays an important role in the early stage of humor processing (incongruity detection). This is supported by previous findings that, compared to healthy subjects, schizophrenia patients have problems in distinguishing between nonsensical and comprehensible punchlines, and these problems are reflected in suppression of the right hemisphere sources activity accompanied with leftward-shifted activity in the fronto-temporo-parietal network (Adamczyk et al., 2019).

At last, we found that patients with longer illness duration more often incorrectly rated absurd punchlines as more comprehensible and more funny. The cognitive abilities correlated in the same fashion with humor comprehension, although no significant relationship between illness duration and cognition was found. Our sample was in the remission phase, which is associated with improved cognitive abilities.
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It is important to note that while cognition remains attenuated and does not deteriorate in remission, humor comprehension does and might be dependent on the initial cognitive abilities of the patient (de la Serna et al., 2013; Buonocore et al., 2018).

Finally, some limitations of our study should be considered before the conclusion. First, this is a correlation study. Therefore, we cannot make any inferences about the causal relationship, i.e., whether the symptoms are responsible for changes in humor processing or vice versa. In addition, we cannot rule out the possibility of some confounding factors that affect either cognition, symptoms, or humor processing. Secondly, we selected only specific literature-based ROIs which have been reported to be relevant to humor comprehension in the healthy population. However, we might have missed some changes in engagement and connectivity between other regions that might be deficient in schizophrenia or engage as compensatory mechanisms. In addition, we used different methodologies to analyze activation (fMRI) and effective connectivity (EEG-DTF) in a complementary fashion. Further studies are necessary to address the questions in a unified/multimodal approach (e.g., activation via EEG-ERP or connectivity via fMRI methods) for a deeper understanding of the neural substrates for the humor-symptom relationship in schizophrenia. Also, in addition to applying FDR correction, we included a number of post hoc analyses without a correction for multiple comparisons. Although these results might limit the type II error and provide better comparison across studies, they should be taken with caution, as they pose an increased risk of type I errors. Next, due to the extensive neuroimaging procedure, we used a brief assessment of cognition. Further studies can focus on further investigating the subcomponents of neurocognition, e.g., verbal learning and fluency, that might be especially relevant for understanding written jokes. Finally, humor is such a complex phenomenon that, given the laboratory conditions, we could only test some limited aspect of it. This experiment is based on Suls’ (1972) and Wyer and Collins’ (1992) model of cognitive structure of humor, based on incongruity detection, which is only one of the hypothetical models. We applied neuroimaging techniques to speculative subcomponents of humor derived from this model, therefore any conclusions must be taken with caution. Nevertheless, while the sample size and the exploratory aspects render the study rather preliminary, it brought novel findings on the neural substrates of humor processing in relation to cognition and psychopathology in schizophrenia, that require further evaluation.

CONCLUSIONS

In summary, we found that humor comprehension is partially associated with the symptom severity and cognitive abilities in schizophrenia outpatients. Our results indicate that impaired cognition and more severe positive and disorganized symptoms were associated with abnormalities in fronto-temporo-parietal activations and effective connectivity that may be regarded as neural underpinnings of observed deficit and its relation to the psychopathology.

ACKNOWLEDGMENTS

We thank all the subjects who participated in this study, to Andrzej Cechnicki for help with providing this work and to Mike Timberlake for proofreading the manuscript.

The work was supported by the National Science Centre, Poland (grants no 2014/13/B/HS6/03091 and 2016/23/B/HS6/00286).

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