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The Processing of Semantic Complexity and Cospeech Gestures in Schizophrenia: A Naturalistic, Multimodal fMRI Study

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Schizophrenia is marked by aberrant processing of complex speech and gesture, which may contribute functionally to its impaired social communication. To date, extant neuroscientific studies of schizophrenia have largely investigated dysfunctional speech and gesture in isolation, and no prior research has examined how the two communicative channels may interact in more natural contexts. Here, we tested if patients with schizophrenia show aberrant neural processing of semantically complex story segments, and if speech-associated gestures (co-speech gestures) might modulate this effect. In a functional MRI study, we presented to 34 participants (16 patients and 18 matched-controls) an ecologically-valid retelling of a continuous story, performed via speech and spontaneous gestures. We split the entire story into ten-word segments, and measured the semantic complexity for each segment with idea density, a linguistic measure that is commonly used clinically to evaluate aberrant language dysfunction at the semantic level. Per segment, the presence of numbers of gestures varied (n = 0, 1, +2). Our results suggest that, in comparison to controls, patients showed reduced activation for more complex segments in the bilateral middle frontal and inferior parietal regions. Importantly, this neural aberrance was normalized in segments presented with gestures. Thus, for the first time with a naturalistic multimodal stimulation paradigm, we show that gestures reduced group differences when processing a natural story, probably by facilitating the processing of semantically complex segments of the story in schizophrenia.

Key words: idea density/gesture/naturalistic stimulation/schizophrenia/semantic processing/multimodal

Introduction

Schizophrenia is characterized by impairments in social interaction and communication, which are often conducted in a multimodal form including auditory speech and hand gestures—two of the most prominent communicative channels in daily situations.[1–6] In schizophrenia, on the one hand, the production and perception of auditory speech at multiple levels of the linguistic hierarchy are impaired.[7–12] On the other, it has been suggested that patients with schizophrenia suffer from a range of dysfunctions in the preparation, execution, perception, and understanding of gestures.[13–19] As a result, impairments in both speech and gesture processing may directly contribute to deficits during multimodal daily communication, i.e., when comprehending information delivered via both gesture and speech. To date, extant neuroscientific studies of schizophrenia have primarily investigated speech and gesture impairments in isolated and strictly-controlled experimental paradigms. It remains unclear how both communication channels are processed (e.g., the observation of gesture, the comprehension of semantics) interactively by patients in an ecologically-valid and naturalistic multimodal context.

Schizophrenia: Dysfunctional Gesture and Speech Processing in a Naturalistic Setting?

Gestures are spontaneous hand movements that deliver either repeating or complementary semantic and pragmatic information in addition to speech. Intact functioning of gestures has a positive impact on daily communication,[20,21] but is often impaired in schizophrenia.[19] In production, patients tend to produce fewer gestures,[22] and they have

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difficulties imitating and producing pantomimes.[13,17,18,23,24] Meanwhile, dysfunctional gesture processing has been reported. Evidence from neuroimaging suggests that patients with schizophrenia showed reduced activation in the inferior parietal lobe and the posterior superior temporal sulcus (pSTS) during observation of gestures; these regions are similarly less activated when they imitate hand gestures.[17] Thus, this parallel neural impairments in both gesture production and observation may indicate a potential aberrance in the putative mirror neuron system in schizophrenia.[25–27] Of note, few other studies showed that patients' processing of hand movements and gestures could remain intact, at least at the neural level. In a study employing a similar paradigm to Thakkar and colleagues, patients showed comparable brain activations for both imitation and observation of hand movements.[28] Similar findings were also observed in our previous studies: When patients process gestures or co-speech gestures (gestures accompanying speech) that are not semantically complex (e.g., iconic gestures), their neural activities remain comparable to that of controls.[16] However, despite the reported normal neural activities when *processing* gestures, patients did show impaired effective brain connectivity between the auditory cortices and the pSTS, when *integrating* speech and gesture, even if the gesture semantics is not as complex, i.e., emblems and pantomimes.[29,30] This could potentially indicate that gesture processing impairments in schizophrenia interact with their potential deficits in higher-order functions such as multisensory integration,[31–34] or the processing of complex semantics.[35,36]

Indeed, at higher-semantic levels, patients' potential impairment in the understanding of gestures is reported to be dependent on language context. For example, when processing gestures in an abstract sentence context (metaphoric gestures), they exhibited impaired behavioral performance to match the semantic information of gesture to a corresponding sentence,[36,37] even more so for those with more severe positive formal thought disorders.[15] In accordance with the behavioral findings, fMRI evidence suggests that, when integrating speech with these metaphoric gestures, patients, as opposed to controls, showed reduced activation in the left inferior frontal gyrus (IFG), as well as reduced functional connectivity between the left IFG and the left STS/middle temporal gyrus (MTG).[16,36]

Despite potential integration difficulties, however, patients could still benefit from a bimodal modality. In a recent fMRI study, we showed reduced neural activation of patients when they process abstract and emblematic speech. However, when the same information is presented bimodally (e.g., co-speech gestures), fMRI results suggest that patients showed comparable brain activations in comparison to controls.[38] These prior studies thus lead to a further research question, that is, whether patients' gesture and speech processing may benefit from a multimodal context, as they would mostly encounter in daily naturalistic situations.

Idea Density as a Window Into Language Deficits in Schizophrenia

A naturalistic approach, which employs ecologically-valid experimental stimulation, has contributed significantly to a sharpened understanding of the neurobiology of language in cognitive neuroscience.[39–42] However, this novel approach hasn't yet been sufficiently exploited in clinical neuroscience research.[12] A core prerequisite of this approach is to parameterize the linguistic/non-linguistic stimuli that participants either produce or process. For linguistic stimuli specifically, such parameterization can be implemented with classical linguistic analyses as well as state-of-the-art computational approaches to language. And clinical and preclinical studies using these methods to analyze patients' language production data have shown great potential in the early detection and prediction of psychosis.[43–46] Of the linguistic approaches, clinicians have commonly used a measure called idea density (ID) to shed light on language dysfunctions in clinical populations. Idea density is a metric of semantic complexity that measures how many propositions are expressed within a specific number of words. Deriving from narratives, its ecological validity enables researchers to investigate cognitive demands and language complexity without interfering directly with the acquisition of experimental data.[47] Idea density is proven informative in investigating the relationship between early linguistic abilities and in predicting the development of Alzheimer's disease,[48,49] mild cognitive impairment,[50] speech impairments of patients with aphasia,[51,52] and aging effects of language.[53–56]

More relevant to the current research, in schizophrenia, idea density has been used to understand patients' higher-order semantic performance.[47,53,57,58] Despite substantial insights, studies on schizophrenia to date have primarily focused on how patients *produce* narratives in either written or oral form; how patients *process* different parts of naturalistic stimuli differing in the degree of semantic complexity has not been studied. Besides, no studies have investigated the neural correlates of the processing of idea density in clinical populations, e.g., in schizophrenia. Prior neuroimaging studies using conventional experimental stimulations (words, sentences) suggest that, when patients process complex semantics, their brain activities in a number of left-lateralized regions including the left IFG,[59–61] the middle frontal gyrus (MFG),[38,62,63] and the left inferior parietal lobe (IPL).[63] However, whether patients with schizophrenia function normally within these regions, when they are presented with more ecologically valid stimuli remains to be tested.

Moreover, prior studies suggest neural facilitation of gesture on speech processing when patients process events delivered with short video clips depicting sentences.[38] But it remains unclear, in a more naturalistic situation, how they might be impaired or benefit from a multimodal context. In a recent study with a healthy college student sample, we examined the processing of a natural, multimodal story with fMRI, and observed a neural facilitative effect (decreased activation of the left middle temporal gyrus) of co-speech gesture when the story is semantically more complex, i.e., when idea density is higher.[64] Potentially, patients could similarly benefit from gestures; however, it is plausible to predict that some language-related regions that are potentially impaired in patients can be differently affected by gestures.

Present Study

In the current study, we employed a naturalistic approach in an fMRI study to investigate neural correlates of dysfunctional speech and gesture processing in schizophrenia. We focused on four specific research questions for the processing of this multimodal story:

1) If the processing of gestures and auditory speech, irrespective of idea density, is impaired in schizophrenia. Based on prior literature, modality-specific activations when processing speech (left-hemispheric fronto-temporal regions) or gesture (bilateral occipito-parietal lobe) could be comparable or different between controls and patients.
2) If, across groups, patients and controls will show neural facilitation (reduced activation of the left middle temporal lobe) from gestures when processing complex stories (high idea density), as shown in Cuevas et al. 2019[64]).
3) If patients are impaired in the processing of semantic complexity of a natural story (as parameterized by idea density). Based on prior fMRI studies of language processing in schizophrenia, we expect to observe reduced neural activation in a number of left-lateralized language-related regions such as the left IFG, the MFG, or the left IPL for complex stories.
4) If a multimodal context (gestures in addition to speech) modulates neural deficits in the regions hypothesized (hypothesis #3) above (if there are any) in schizophrenia.

Methods

Participants

We summarized participants' demographic and clinical characteristics in table 1. Sixteen patients were recruited at the Department of Psychiatry and Psychotherapy at the Philipps University of Marburg, and were diagnosed according to ICD-10 with schizophrenia (F20.0, n=12, and F20.3, n=1) or schizoaffective disorder (F25.0, n=2, and F25.2, n=1). Participants in both groups are native speakers of German. All except one patient received antipsychotic treatment; six were additionally treated with antidepressant medication. Positive and negative symptoms were assessed with the Scale for the Assessment of Positive Symptoms (SAPS) and the Scale for the Assessment of Negative Symptoms (SANS). Eighteen age–, gender–, and education-matched healthy participants with no history of any mental disorders were recruited from the same area. This is an independently recruited new sample and none of the controls were included from Cuevas et al. 2019[64]). Exclusion criteria for both groups were brain injury and neurological or other medical diseases affected by brain physiology. In both groups, we conducted neuropsychological tests to assess working memory function, digit span, trail making (TMT), verbal IQ (MWT-B),[65] and gesture production and perception (BAG, Brief Assessment of Gesture.[66] These measures are reported in table 1. All participants had normal or corrected-to-normal vision and hearing. Except for one control and one patient, all other participants are right-handed. All participants gave written informed consent prior to participation in the experiment and were compensated monetarily. The study was approved by the ethics committee of the School of Medicine, Philipps University Marburg.

Table 1. Demographic, Medication, Symptom, and Neuropsychological Measures

	Patients (n = 16)	Controls (n = 18)
Age (years)	34 (12.18)	31.94 (10.21)
Gender male/female	13/3	13/5
Education (years)	11.81 (1.83)	12.72 (1.36)
TMT A (seconds)	31.47 (11.08)	26.17 (9.89)
TMT B (seconds)	69.30 (39.01)	52.93 (19.58)
Digit Span forward	7.75 (1.61)	8.05 (2.43)
Digit Span backward	6.00 (1.31)	6.61 (2.50)
Verbal IQ	28.87 (5.42)	28.5 (3.79)
BAG subscores	3.20 (0.53)	3.37 (0.46)
SAPS (global)	15 (6.89)	
SANS (global)	9 (6.02)	
CPZ Equivalent	562.52 (372.63)	

Note: Values are presented as mean (SD). Pairwise t-tests for all reported measures were non-significant (all P-values > .12). TMT, trail-making test; CPZ, chlorpromazine.

Stimuli

All participants were presented with 16 video clips depicting an actor (figure 1) narrating consecutive parts of a slightly modified version of the short story "Der Kuli Kimgun".[67] The story was unfamiliar to all participants. The trained actor narrated the story naturally and performed spontaneous gestures of any kind (iconic, metaphoric, beat, and emblematic) using hands and arms. The actor decided freely the moment and the way to make the gestures, which were all congruent with the semantic content of the story. The presentation of the

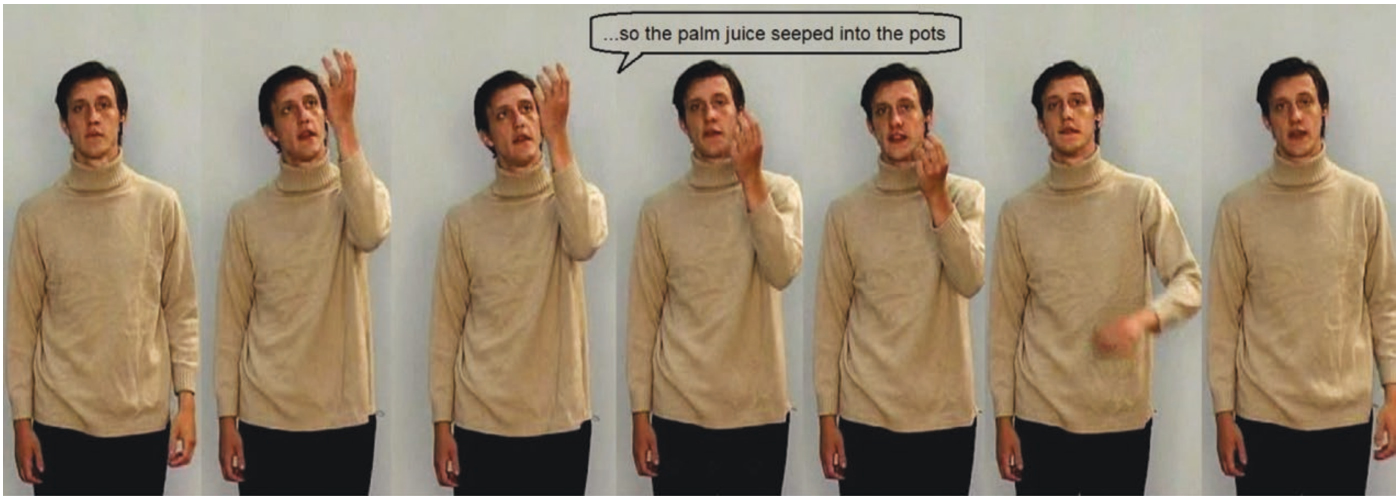

Fig. 1. Example of stimuli. Seven still frames of the video illustrate how the actor performed the gestures.[64] A short segment of the story was translated into English and depicted in the speech bubble for illustrative purposes. The actor moved his fingers in the air while moving down his arm, indicating how the liquid (palm juice) ran down into the pots.

videos lasted 32:12 minutes, with individual clips lasting between 1:02 and 3:31 minutes (for detailed information, see Cuevas et al. 2019; 2020[64,68]).

Experimental Design and Procedure

The entire story was divided into 330 segments of 10 words each, in order to identify parts of the story with low or high semantic complexity. As there were jitter periods of 6–14 seconds between videos, we excluded text segments that included the end of one video and the beginning of the next one from the analysis. Then, the semantic complexity of each 10-word-segment was measured by the ID. We refer to the manual by Chand *et al.*[69] The calculation of the ID value is based on the number of propositions (ideas) in a text, then dividing them by the number of total words, and multiplying the result by 10. For example, for the sentence 'Samir was a poor, Indian boy, as poor as the dust on the country road', we could identify four ideas 'Samir was a boy', 'boy, poor', 'boy, Indian', and 'as poor as the dust'. (for more details about the calculation, see Cuevas et al. 2019[64]). Accordingly, the higher ID of a segment would imply that it is semantically more complex. Every segment of the story had an ID value between two and nine (mean: 5.35 SD: 1.12). The segments with an ID value of five or below were counted as low complexity segments and segments with a value of six or higher were considered as high complexity ones. In the literature, there is no established value that can serve as a standard or reference of average complexity. This is due to the fact that in the case of language production, ID values are influenced by the size of the analyzed text and the number of subjects participating in a study.[70] Other studies concerning ID in language production have defined high values as the top two-thirds and low values as the bottom third.[49] However, here we decided to divide the values into just two categories to create an equal split of four values each (i.e., 2–5 and 6–9).

In addition, each segment included between zero and four gestures (mean: 1.50, SD: 0.82). The number of gestures appearing in each segment did not differ significantly between the low- and high-ID conditions (see Cuevas et al. 2019[64]). Gestures that occurred between two segments were counted twice: once in the segment where they started, and once in the segment where they ended. Based on the ID value (low vs. high) and the number of gestures per segment, six different conditions were defined: zero gestures (low_noG, high_noG), one gesture (low_1G, high_1G), and two or more gestures (low_2+G, high_2+G). No significant interaction for the number of trials and segment duration was found between the factors *gesture* and *ID*. However, we had fewer trials without gestures and longer duration for the high complexity conditions. This was regarded as unproblematic as our analyses focused on the interaction between both factors (for the complete description of the stimulus material, see Cuevas et al. 2019.[64]

During the acquisition of fMRI data, participants were asked to attend to the videos (presented through a mirror mounted on the head coil) and to watch and listen to the actor carefully, without engaging in any online tasks. Air conduction headphones (Siemens) were used for the presentation of verbal information. The loudness of the headphones was kept constant across sessions. In order to make sure that the subjects listened to the narrative, they were asked to answer a questionnaire containing details of the story (e.g., critical moments, narrative shifts, etc.).

fMRI Data Acquisition

All images were acquired using a 3-Tesla Siemens scanner (Siemens MRT Trio series). The functional images were obtained using a T2*-weighted echo-planar image sequence (TR = 2 s, TE = 30 ms, flip angle = 90°, slice thickness = 4 mm, interslice gap = 0.36 mm, field of view = 230 mm, matrix = 64 × 64, voxel size = 3.6 x 3.6 x 4.0 mm, 30 axial slices orientated parallel to the AC-PC line). 970 functional images were acquired (450 during the first run and 520 during the second run). The first acquisition run lasted 15 minutes and the second one lasted 17 minutes and 20 seconds, due to the varying lengths of individual videos. Simultaneously to fMRI data, additional EEG data were acquired. These data were intended to be used for another research project and will not be further discussed here.[71, 72] The use of an EEG cap was not expected to affect the quality of the BOLD responses.[73]

Data Analysis

The MRI images were analyzed using Statistical Parametric Mapping (SPM12; www.fil.ion.ucl.uk) implemented in MATLAB 2009b (Mathworks Inc. Shevorn, MA). To minimize T1-saturation effects, the first two volumes were discarded from the analysis. Afterward, all images were registered to the first image of the first run and co-registered to the anatomical volume, normalized into MNI space (voxel size = 2 x 2 x 2 mm), and smoothed with an 8 mm isotropic Gaussian filter. A high-pass filter (cut-off period 128 sec) was used. Statistical analysis was performed in a two-level procedure. The design matrix for the modulation of single-subject BOLD responses at the first level comprised the onsets and durations of all six conditions, as well as the six movement parameters of each subject. The hemodynamic response function (HRF) was modeled by the canonical HRF. A flexible factorial second-level analysis with six conditions (low_noG, low_1G, low_2+G, high_noG, high_1G, high_2+G) was performed.

A Monte Carlo simulation of the brain volume of the current study was employed to determine an adequate voxel contiguity threshold.[74] It is suggested that this correction provides sensitivity to smaller effect sizes and also corrects for multiple comparisons across the whole brain volume.[75] Assuming an individual voxel type 1 error of $P < .001$, a cluster extent of 87 contiguous resampled voxels was indicated as necessary to correct for multiple comparisons at $P < .05$. Thus, clusters with at least 87 voxels and a significance level of $P < .001$ are reported for all contrasts. All described coordinates of activation are located in MNI space. The AAL toolbox[76] was employed for the anatomical localization of the clusters.

Contrasts of Interest

We firstly tested for general group differences in the neural processing of the narrative and group differences in the processing of gestures (*group x gesture*). We also tested, across groups, if gesture facilitates the processing of story differing in complexity (*gesture x complexity*), as have been observed in Cuevas et al. 2019; 2020.[64, 68] Then, we focused on the between-group difference in the processing of story segments differing in ID (*group x complexity*). Lastly, we tested the interaction of *group x complexity x gestures* to test if group-specific processing of semantic complexity may be modulated by the presence of co-speech gestures.

Results

We found no significant main effect of *group* and no group differences regarding the processing of gestures. Post-hoc tests revealed an activation increase in both groups during the processing of co-speech gestures (*Speech + Gesture [gesture:1&2+] > Speech [gesture:0]*) in the bilateral occipito-parietal regions (figure 2B, and supplementary table 1s). The activation in this cluster increased according to the number of gestures presented, similarly across both groups, as suggested by the results from the conjunction analysis between controls and patients (supplementary figure 1s, supplementary table 3s). Post Hoc mixed-ANOVA based on the extracted eigenvariate in this region showed no interaction of *group x gesture* ($F_{(2, 64)} = 2.79$, $P = 0.07$, $np^2 = 0.08$), but a significant main effect of gesture ($F_{(2, 64)} = 52.51$, $P = 3.18e\text{-}14$, $np^2 = 0.62$).

The reverse contrast (*Speech [gesture:0] > Speech + Gesture [gesture:1&2+]*) indicates that gestures resulted in group-independent reduced activation of the left MTG, the left IFG, and the right caudate (see figure 2A and supplementary table 1s). Again, conjunction analysis suggests that left MTG activation is comparable across groups (supplementary figure 1s for the left MTG activation, supplementary table 3s, for details). Post Hoc mixed-ANOVA based on the extracted eigenvariates in the left MTG showed no interaction of *group x gesture* ($F_{(2, 64)} = 0.08$, $P = 0.92$, $np^2 = 0.002$), but a significant main effect of gesture ($F_{(2, 64)} = 5.52$, $P = 0.006$, $np^2 = 0.15$).

The contrast *gesture x complexity* showed that gesture reduced the activation in the left temporal lobe, the cerebellum, and the Herschel gyrus, when semantic complexity is high (high-ID), as shown in figure 3 and supplementary table 2s. Post Hoc repeated-measures ANOVA based on the extracted eigenvariates in the left anterior temporal lobe showed a significant interaction of *gesture x complexity* ($F_{(2, 66)} = 12.81$, $P = 2.0e\text{-}6$, $np^2 = 0.28$). The findings are direct replication of our previous studies with different samples.[64,68]

The contrast *group x complexity* revealed that, in comparison to controls, patients showed reduced activation in the left IPL when ID is high; however, in the low ID passages, the left IPL activation in patients was higher than that of controls (figure 4 and supplementary table 1s). Post Hoc mixed-ANOVA based on the extracted eigenvariates in the left IPL showed a significant interaction of *group x complexity* ($F_{(1, 32)} = 7.46$,

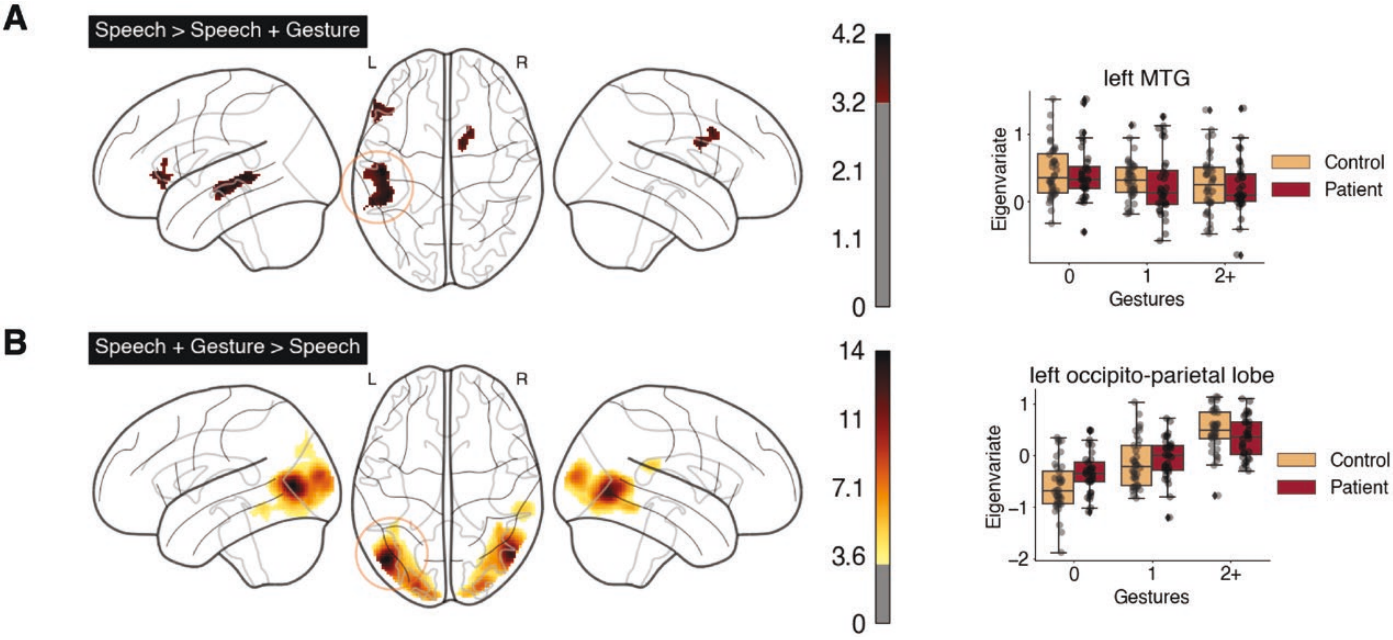

Fig. 2. Gesture-related activation decrease and activation increase in both groups. (A) Contrast of [Speech > Speech + Gesture] as shown in the glass brain (left panel) and boxplots (right panel) showing eigenvariates extracted from the cluster that peaks at the left middle temporal gyrus (left MTG, [–48, –16, –10; k = 444]). (B) Contrast of [Speech + Gesture > Speech] as shown in the glass brain (left panel) and boxplots (right panel) showing eigenvariates extracted from the cluster that peaks at the left occipital lobe [–46, –72, –6; k = 4092]. For all glass brain figures, the threshold for voxel activations was set at $P < .001$ uncorrected, and only clusters larger than 87 voxels have been included (Monte-Carlo cluster-extent corrected at $P < .05$). Color bar indicates the scale of the T-statistics. Speech: Gesture = 0; Speech + Gesture: Gesture = 1 & 2+.

$P = 0.01$, $np^2 = 0.19$). We also reported within-group comparisons for High-ID > Low-ID comparisons in the supplementary figure 2s. There, results revealed no significant activations for patients. For controls, this contrast activated the right superior/inferior parietal lobe.

Lastly, the interaction *group x complexity x gesture* (figure 5, supplementary table 1s) activated the bilateral IPL and the middle frontal gyrus (MFG), and additionally the right IFG. Here, in these regions, the activation increase for higher ID passages (high-ID > low-ID) was observed only when no gestures were presented (Gestures = 0). When the story was presented in a multimodal form (Gestures = 1 & 2+), this high-ID > low-ID difference was normalized for patients. Post Hoc mixed-ANOVA based on the activation increase (high-low) in the left IPL showed significant interaction of *group x gesture* ($F_{(2, 64)} = 8.32$, $P = 0.0006$, $np^2 = 0.21$); this interaction is also significant in the right MFG ($F_{(2, 64)} = 15.68$, $P = 3.0e-7$, $np^2 = 0.32$).

Discussion

In the current study, we investigated if patients with schizophrenia are impaired in the neural processing of semantic complexity within a naturalistic multimodal context. Our results suggest that patients, in comparison to controls, showed increased activation of the left IPL during the processing of semantically less complex passages; however, the left IPL activation was reduced for patients when semantic complexity was high. More importantly, the presentation of gestures reduced this group difference, suggesting a facilitative or compensatory role of gestures in this context.

The Processing of Gesture is Comparable Between Groups

For both groups, the *Speech + Gesture > Speech* comparison activated the bilateral posterior occipito-parietal visual regions, thus suggesting that patients are comparable to controls in recruiting this region to process gesture when processing naturalistic stimuli, in a similar way to isolated bimodal videos.[36,64,72,77,78] These findings may imply that, despite well-documented gesture dysfunctions in schizophrenia,[17,79] the perception of gestures *per se* in schizophrenia, at least at a neural level, could appear to be largely intact (Horan et al. 2014[28]), especially when patients are engaged in a high-level context where potential higher-level processing could be impaired (i.e., presented together with speech in both isolated and naturalistic multimodal settings). However, this finding doesn't rule out the possibility that gesture imitation and production is neurally impaired in schizophrenia,[13,17,80] or that their impairment in gesture observation/perception may present at the behavioral

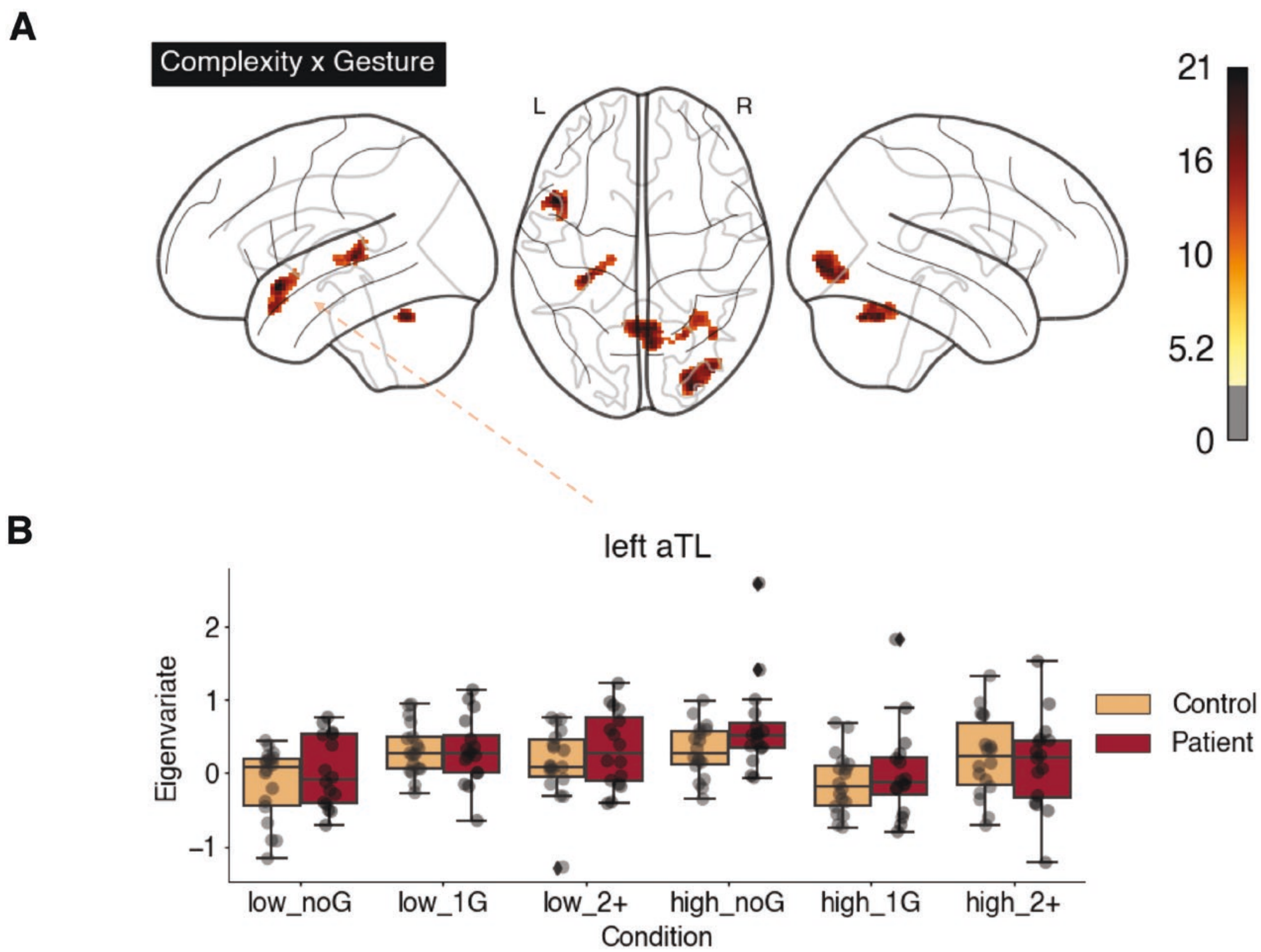

Fig. 3. Interaction *gestures x complexity*. (A) Activation clusters localized in the anterior temporal lobe (aTL), inferior occipital gyrus, cerebellum and Herschel gyrus. (B) Boxplots showing reduction of activation at the anterior temporal pole during the high complexity conditions when gesture was presented [high_1G, high_2+]. The threshold for the glass brain figure was set at $P < .001$ uncorrected, and only clusters larger than 87 voxels have been included (Monte-Carlo cluster-extent corrected at $P < .05$).

level.[14,81,82] Besides, given that the sample size of the current study is moderate, interpretation of this null effect warrants caution.

Results from the *Speech > Speech + Gesture* comparison are in accordance with our prior studies,[64,68] and suggest that segments without gestures may recruit more neural resources in the left hemispheric speech and language regions (e.g., the left IFG and MTG). Importantly, this facilitative effect of gesture, irrespective of semantic complexity, was present for both patients and controls, thus suggesting that gesture may facilitate story comprehension in general in both healthy populations and in patients schizophrenia, echoing findings from a range of behavioral and neuroimaging studies.[3,20,38,83] Below, we present evidence that gesture's facilitation effect on speech processing can be complexity-specific.

Aberrant Neural Processing of Semantic Complexity in Schizophrenia is Modulated by Gesture

In direct accordance with our previous study,[64,68] when collapsing across patients and controls, we observed that gesture modulates the brain activity at the left temporal lobe (aTL and MTG) in response to the processing of high complexity passages. This finding, together with our previous studies with other samples,[64] concurs with the role of the left temporal regions in language processing,[84,85] but additionally provides the proof—with a naturalistic stimulation—that gesture may positively interfere speech comprehension when the stimuli are semantically complex.

The focus of this study was on potential impairments when patients with schizophrenia process the naturalistic multimodal story differing in the degree of semantic

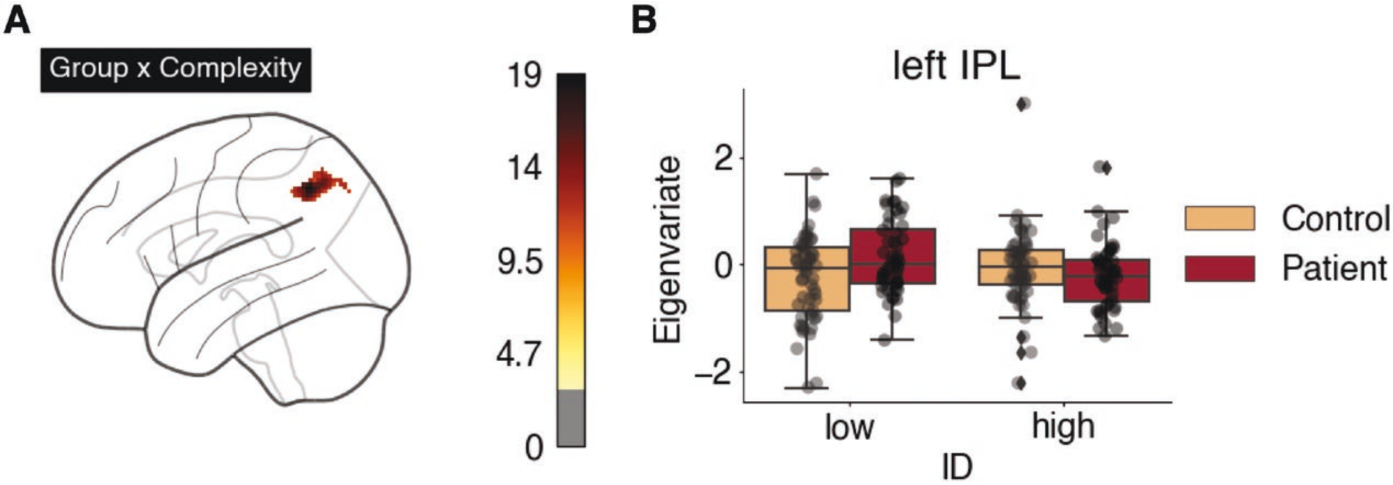

Fig. 4. (A) Interaction *group x complexity* shown in the glass brain figure. (B) Boxplots showing eigenvariates extracted from the cluster that peaks at the left inferior parietal lobe (left IPL, [–52, –54, 44; k = 149]). The threshold for the glass brain figure was set at $P < .001$ uncorrected, and only clusters larger than 87 voxels have been included (Monte-Carlo cluster-extent corrected at $P < .05$). Color bar indicates the scale of the F-statistics.

complexity. Indeed, when collapsing across all gesture conditions (gesture: 0, 1, 2+), patients, as opposed to controls, showed increased activation for the low complexity and decreased activation for high complexity passages in the left IPL. Moreover, when the factor of gesture is considered, we observed that this effect interacts with gesture in the bilateral IPL and additionally the middle frontal regions. Specifically, the neural aberrance in these regions (including the left IPL) was only present when no gesture was presented. In contrast, when the story was presented in a multimodal form (gesture: 1 and 2+), group differences were largely not observable.

The left IPL is an important region that underlies a range of cognitive functions that are functionally relevant to human social communication.[86,87] Importantly, the left IPL is crucially involved during language comprehension at the semantic level,[84,88] and has been reported to support semantic prediction during comprehension of a naturalistic auditory story.[42] Besides, the left IPL is associated with working memory and is sensitive to the cognitive load of the task.[89] In schizophrenia, the left IPL activity is reported to be reduced for patients when they are engaged in sentence-level language comprehension tasks.[63] In the current study, although patients showed even increased activation in the left IPL in the low-complexity passages, when they processed parts of the story that are semantically more complex, they failed to activate the left IPL as controls did. This neural aberrance, during the processing of a naturalistic narrative, might derive from patients' impaired working memory capacity and semantic processing.[7,90–92]

Besides the left IPL, beyond our hypothesis, the three-way interaction also showed that gesture normalized the activation of the right IPL, the bilateral MFG, and the right IFG, despite the fact that these regions were not activated in the group x complexity contrast. This might be an indication that the right homologs of the left-hemispheric language-related regions could benefit especially from the presentation of gestures. The right IPL impairments have been related to a range of sensory and cognitive dysfunctions in schizophrenia;[93] right IPL impairments in schizophrenia may also underlie deficits in both semantic processing and gesture processing.[94–96] Regarding the right IFG, clinical neuroscientific literature often reports increased activation in this region and regards this pattern as a proof for reduced lateralization in schizophrenia.[97,98] However, reduced activation in the right IFG (together with enhanced activation in the left IFG) has also been reported for schizophrenia when patients engage in the processing of complex semantics such as metaphor.[99] Thus, our results may imply that these right-hemispheric regions could especially benefit from an additional modality when patients process semantically complex segments. However, the exact role of the right hemisphere in multimodal language processing in schizophrenia would require further research.

The MFG is associated with the maintenance of verbal information.[100] In this regard, participants might recruit this region, especially during the complex speech conditions because multiple semantic events have to be kept in mind in order to interpret the entire story. Nevertheless, patients recruit this region already even to a higher degree than controls, during the low complexity speech condition. However, in the high complexity condition, the left MFG activity in patients was reduced. Notably, a study investigating the processing of novel and conventional metaphors by patients with schizophrenia also reported increased activation of the left MFG.[99] There, the activation decreased as the cognitive demands of the task increased (in this case abstract thinking). Previous

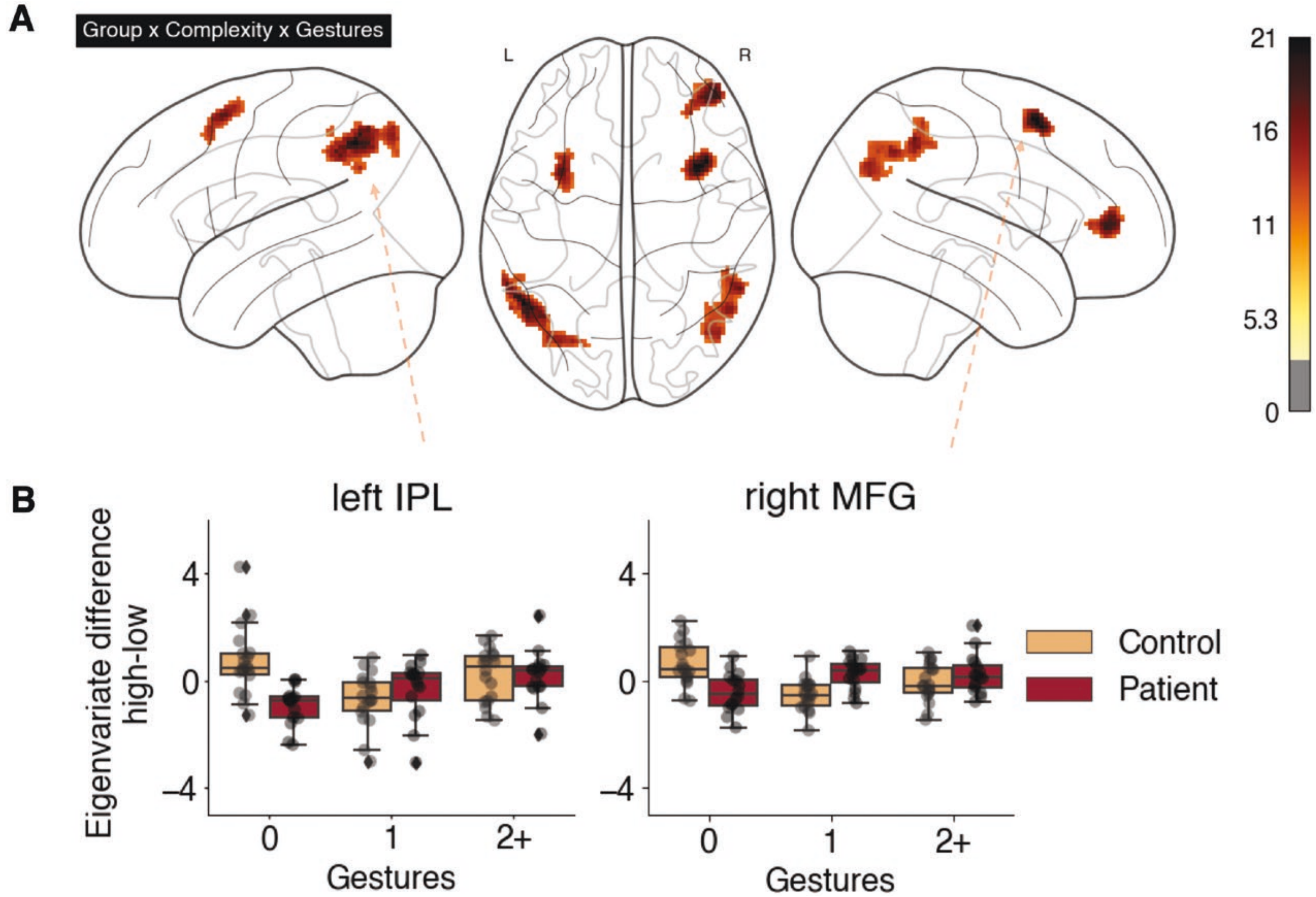

Fig. 5. (A) Interaction *group x complexity x gestures* shown in the glass brain figure. (B) Boxplots showing the difference of eigenvariates between high-ID and low-ID conditions, extracted from the clusters that peak at the left inferior parietal lobe (left IPL, [–50, –56, 46; k = 367]), and the right middle frontal gyrus (right MTG [–34, 12, 58; k = 181]). The threshold for the glass brain figure was set at $P < .001$ uncorrected, and only clusters larger than 87 voxels have been included (Monte-Carlo cluster-extent corrected at $P < .05$). Color bar indicates the scale of the F-statistics.

studies also suggest close.link between working memory and the processing of co-speech gestures.[101] Thus, in our study, patients' activation in this region decreased as the demands of the narrative increased, i.e., in high complex passages. On the other hand, the right MFG plays an important role in the temporal sequencing of discourse,[102] an ability that is fundamental for interpreting the story.

Together, the increased activation by patients during the low complexity condition indicate that patients already need more neural effort (increased BOLD response) for the processing of low complexity segments; when the story is semantically too complex (high-ID), patients then failed to provide the necessary resources in these regions (reduced BOLD response). However importantly, this neural aberrance was only observable when there was no gesture presented together with speech. In contrast, in these regions, whenever the story was presented in a multimodal form (gesture: 1 and 2+), the activation pattern is comparable between groups. A similar facilitative effect of gesture when processing a story has been observed for elder vs. younger participants, i.e., group difference was reduced when gestures were presented together with story segments.[68] In line with these findings, for isolated sentences, despite the fact that patients showed neural aberrance when processing abstract-social gestures and concrete-non-social speech, group difference was significantly reduced when these events were presented in a multimodal form.[38] In the current study, we extend prior findings by showing a similar facilitative nature of gesture during speech comprehension: In a naturalistic story setting, even if patients' neural aberrance may be more likely to derive from their impaired semantic prediction and working memory capacity, which are not as heavily demanded in isolated situations, nevertheless, a multimodal context is, again, proven beneficial.[3,20]

Limitation

Despite new insights, the current study has clear limitations. Limited by the sample size of this study ($n = 16$ &

18 for each group), we are unable to test the role of medication for story comprehension, and cannot pinpoint if the observed neural aberrance (as well as neural facilitation) is specific to chronic or first-episode schizophrenia. Another limitation regarding the current study is that, during the experiment, participants are not engaged in any online behavioral tasks, nor did we set up any measurements (e.g., eye-tracking) that track participants' attention to the multimodal story. While it could be an advantage that participants are not engaged in online behavioral tasks where additional affordances might interfere with processing and thus provoke group difference, this is nevertheless a drawback that limits our interpretation of patients' potential speech/gesture processing deficits (and the normalization of gesture) at the neural level. Evidently, future studies should consider a dynamic combination of behavioral and neuroimaging methods, especially when delivering naturalistic stimulations. Lastly, although our stimulation is naturalistic in the sense that it is both multimodal and narrative,[103] this paradigm is not a direct approximation of the majority of real-life situations such as conversations.[3,104,105] These emerging studies in basic science could provide examples for future neuroscientific research of psychosis.

Conclusion and Future Research

The following conclusions can be drawn from this naturalistic experiment: First, patients and controls recruit similar regions for the processing of gestures and speech in general. Second, patients, when compared to controls, show reduced activation in the bilateral middle frontal and parietal regions when processing parts of the story that are semantically more complex. Finally, gestures reduced group differences, potentially by facilitating the processing of the narrative. Thus, future studies could examine if the differences in the processing of semantic complexity are reduced by conducting existing training developed to improve verbal communication and social cognition.[106,107]

Supplementary Material

Supplementary data are available at *Schizophrenia Bulletin Open* online.

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