

Contents lists available at [ScienceDirect](http://www.sciencedirect.com)

Schizophrenia Research

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

Altered lateralisation of emotional prosody processing in schizophrenia

Dominik R. Bach^{a,c,*}, Marcus Herdener^a, Didier Grandjean^b, David Sander^b,
Erich Seifritz^{a,1}, Werner K. Strik^a^a University Hospital of Psychiatry, University of Bern, Bolligenstrasse 111, 3000 Bern 60, Switzerland^b Swiss Center for Affective Sciences & Department of Psychology, University of Geneva, 7 rue des Battoirs, 1205 Geneva, Switzerland^c Wellcome Trust Centre for Neuroimaging, University College London, 12 Queen Square, London WC1N 3BG, United Kingdom

ARTICLE INFO

Article history:

Received 3 July 2008

Received in revised form 19 January 2009

Accepted 3 February 2009

Available online 13 March 2009

Keywords:

Lateralization index

LI

Emotional

Affective

Prosody

Language

Paranoid schizophrenia

ABSTRACT

Alterations of cerebral lateralisation in schizophrenia have been reported consistently, and a reduced left-lateralisation has been suggested for language functions. Speech contains non-verbal information, e.g. prosody, and on a behavioural level, the extraction of emotional information from prosody is often impaired in schizophrenia. A previous functional magnetic resonance imaging study suggests increased left-lateralisation in schizophrenia during prosody processing, but did not disentangle effects of speech processing as such and emotional prosody processing. Here, we used meaningless syllables spoken with neutral, angry or fearful speech melody and measured blood oxygen level-dependent (BOLD) responses in 15 in-patients with schizophrenia and 15 healthy control participants matched for age and gender. Lateralisation indices were calculated for responses to emotional versus neutral prosody, and for all types of prosody versus baseline. Compared to control participants, patients with schizophrenia showed an increased right-lateralisation of emotional and non-emotional prosody processing in the temporal and parietal cortex. This right-lateralisation was increased in patients with reduced right-handedness and decreased in patients with stronger negative symptoms, particularly affective blunting, and with longer hospitalisation. Although patients with schizophrenia performed worse in emotion identification, this deficit was not related to lateralisation indices. Enhanced right-lateralisation to prosody resembles previous findings on laterality changes in speech processing and might suggest a common underlying cause in the organization of language functions.

© 2009 Elsevier B.V. All rights reserved.

1. Introduction

Altered cerebral lateralisation of patients with schizophrenia has consistently been reported regarding handedness, brain anatomy, and language functions (Sommer et al., 2001). With respect to speech generation and perception, functional neuroimaging and behavioural (i.e. dichotic listening) studies converge towards a reduced left-lateralisation, or increased right-lateralisation, as compared with the normal

population (Li et al., 2007; Ngan et al., 2003; Razafimandimby et al., 2007; Sommer et al., 2001; Spaniel et al., 2007; Woodruff et al., 1997). Spoken language contains a speech melody, or prosody, that can allow inferring the speaker's feelings (Grandjean et al., 2006; Scherer, 2005). Patients with schizophrenia are often impaired in the capability to extract such non-verbal emotional information from language (see for example Bach et al., in press; Edwards et al., 2001, 2002; Kucharska-Pietura et al., 2005; Leitman et al., 2005).

Surprisingly, a functional magnetic resonance imaging (fMRI) study by Mitchell et al. (2004) suggested an increased left-lateralisation of cerebral responses to emotional prosody in patients with schizophrenia. As this study compared prosody perception against baseline, emotional prosody processing was confounded with more general aspects of speech processing.

* Corresponding author. Wellcome Trust Centre for Neuroimaging, 12 Queen Square, London WC1N 3BG, United Kingdom. Tel.: +44 20 7833 7472.
E-mail address: d.bach@fil.ion.ucl.ac.uk (D.R. Bach).

¹ Current affiliation, Clinic for Affective Disorders and General Psychiatry, Psychiatric University Hospital, Lengstr. 31, 8032 Zurich, Switzerland.

Hence, results of this study are somewhat contradictory to the *reduced* left-lateralisation in patients with schizophrenia that is commonly found in response to speech.

In order to circumvent this confound, the purpose of the present study was to compare lateralisation of neural responses to emotional and to neutral prosody in schizophrenia and healthy individuals. Robust lateralisation measures in fMRI have been proposed and successfully used, e.g. in the estimation of lateralised responses in basic auditory perception (Devlin et al., 2003), language perception (Jansen et al., 2006; Wilke and Lidzba, 2007), and neutral speech perception in schizophrenia (Li et al., 2007; Razafimandimby et al., 2007; Spaniel et al., 2007). The advantage of such measures is that instead of analysing brain responses on a voxel-by-voxel basis, which might overlook differences that are slightly below significance thresholds, they search for a pattern of responses.

Evidence for a prosody recognition deficit in schizophrenia comes from tasks examining explicit appraisal of emotional content in prosody. Social interaction however might require implicit appraisal of emotional prosody (Bach et al., in press). Therefore, we gave both implicit (gender identification) and explicit (emotion identification) task instructions and tested for potential differences between the appraisal levels.

Since there is some evidence that the prosody recognition deficit is dependent on schizophrenia subtype (Edwards et al., 2002), we aimed at limiting our findings to the most frequent subgroup, that is, paranoid schizophrenia, as defined by ICD-10 (WHO, 2004). Taking into account previous reports from studies investigating lateralisation in speech processing and prosody processing, we hypothesised that laterality measures related to emotional prosody would differ between groups in the temporal and parietal lobe.

2. Materials and methods

2.1. Participants

Fifteen in-patients with paranoid schizophrenia and 15 healthy participants were recruited for this study. The control group was completely independent from a previous study using a similar paradigm (Bach et al., 2008a). All participants were right-handed and had German as their first language. Exclusion criteria for all participants were psychiatric comor-

Table 1
Sociodemographic data of the study participants.

	Healthy control participants	Patients with paranoid schizophrenia
Age (mean \pm SD)	31.5 \pm 7.9	31.6 \pm 7.9
Gender	8 male, 7 female in each group	
Edinburgh Handedness Quotient	81.7 \pm 14.3	79.5 \pm 16.3
<i>Secondary education (%)</i>		
<9 years, or no degree	0%	6.7%
9 years degree	26.7%	66.7%
12 years degree	73.3%	26.7%
<i>Tertiary education (%)</i>		
None	40%	66.7%
Occupational degree	40%	33.3%
University degree	20%	0%

Table 2
Illness-related characteristics of patients with schizophrenia.

Time since first symptoms in months (median)	76
Time since first hospitalisation in months (median)	20
Duration of current hospitalisation in weeks (median)	5
Number of previous hospitalisations (median)	3
Percentage of patients receiving antipsychotic drugs	100%
First generation (Zuclopenthixol, Flupenthixol)	13.3%
Second generation (Risperidone, Clozapine, Quetiapine, Olanzapine, Amisulpride)	93.3%
Third generation (Aripiprazole)	6.7%
Percentage of patients receiving benzodiazepines	13.3%
Percentage of patients receiving anticonvulsant mood-stabilizers	6.7%
Chlorpromazine equivalent dose (mg CPZ, mean \pm SD)	462.1 \pm 408.5
PANSS P-subscale (mean \pm SD)	13.3 \pm 6.2
PANSS N-subscale (mean \pm SD)	16.3 \pm 6.3
PANSS G-subscale (mean \pm SD)	23.9 \pm 6.1

idity, known organic brain damage, mental retardation, epilepsy, current substance abuse, auditory impairments, and the usual MRI exclusion criteria. Handedness was assessed using the Edinburgh Handedness Inventory (Oldfield, 1971).

Diagnosis of paranoid schizophrenia was made by the treating clinician and confirmed by a clinically trained member of the study group (DRB) according to ICD-10 (WHO, 2004). To ensure a stable diagnosis, it was required that the retrospectively assessed onset of first symptoms was more than a year ago. Symptoms were assessed on the study day with the Positive and Negative Symptom Scale, coding from 1 to 7 for each symptom (PANSS; Kay et al., 1987). All patients were approached as soon as the treating clinician judged them to be able to maintain attention for the required amount of time (about 60 min). Healthy control participants were recruited from the general population by advertisement and were given a monetary reward for their participation.

The two groups were matched one-by-one for gender and age with a maximum difference of five years within each couple. Sample characteristics are listed in Tables 1 and 2. All participants gave written informed consent, and the study was approved by the ethics committee of the canton of Bern.

2.2. Stimulus material and tasks

Stimuli were constructed as described previously (Bach et al., 2008a) from the set of Banse & Scherer (1996). Eight speakers (four female, four male) were selected from the set, and for each speaker and each emotion, three excerpts of 750 ms were cut that contained the pseudo-words “*fee gott laish*”, “*gosterr*”, and “*nyou venzy*”. This procedure resulted in 24 stimuli for every emotion category *anger*, *fear*, and *neutral* that were normalised with respect to mean sound pressure level. For each of the two fMRI tasks, these 72 stimuli were presented via headphones (Commander XG, Resonance Technology, Northridge, CA, USA) in pseudo-random order, including 24 interspersed null events. During twelve discarded fMRI volumes at the start of each run (36 s), three extra habituation items were presented, followed by 18 s of silence. The experiment was programmed in e-prime (Version 1.1.4.4, Psychology Software Tools, Pittsburgh, PA, USA).

Subjects were asked in the first task to discriminate the speaker's gender and give a key response as quickly as possible, and in the second task to discriminate the emotion

of the speaker. Instructions were explained before each task and were visible all the time using a mirror/screen system.

2.3. Imaging

Images were acquired on a 3 T scanner (Trio, Siemens, Erlangen, Germany). Anatomical T_1 -weighted images were obtained with a three-dimensional magnetization-prepared rapid acquisition gradient echo sequence (MPRAGE) at a voxel size of 1 mm^3 (repetition time TR , 1950 ms; echo-time TE , 2.15 ms). The fMRI data were acquired using blood oxygen level-dependent (BOLD) signal-sensitive T_2^* -weighted gradient-recalled echo-planar imaging (EPI; TE , 30 ms; TR , 3000 ms; acquisition time TA , 2000 ms). Two series of 210 functional whole-brain volumes consisting of 30 contiguous slices 4 mm thick positioned in the intercommissural plane (field of view, $230 \times 230\text{ mm}^2$; matrix, 64×64 pixels) were acquired. The first twelve volumes of each series were discarded. With a TR of 3000 ms and a TA of 2000 ms, a silent gap of 1000 ms resulted between each acquisition. In every second silent gap, either a prosodic stimulus (750 ms) was presented, or this interval was defined as null-event (silence). Within these 1000 ms gaps, stimulus onset delay varied randomly between 50 ms and 200 ms.

2.4. Data analysis: behavioural responses

Behavioural responses were analysed in a 3 (emotion) \times 2 (task instruction) \times 2 (group) analysis of variance (ANOVA) model, using the general linear model approach in SPSS (Version 12, SPSS Inc., Chicago IL, USA).

2.5. Data analysis: statistical parametrical maps

Image analysis was performed using statistical parametric mapping (SPM 5; Wellcome Trust Centre for Neuroimaging, London, UK; www.fil.ion.ucl.ac.uk/spm) on Matlab (Version 7.1., MathWorks, Natick, MA, USA). For intra-run realignment, the MR-scanner manufacturer's online motion correction was used. Functional images were realigned between runs, corrected for slice timing, normalized to the Montreal Neurological Institute (MNI) T_1 -weighted brain template (resampled voxel size: $2 \times 2 \times 2\text{ mm}^3$), and spatially smoothed (8 mm isotropic full width at half maximum Gaussian kernel) using standard procedures in SPM 5. Onsets for each of the six event types were modelled as a stick function, convolved with a canonical hemodynamic response function. Individual reaction times and the mean fundamental frequency F_0 (calculated with Praat; Version 4.5, www.praat.org) for each event were taken into the model as two additional regressors. Statistical parametric maps were generated from contrasts of interest (main effect emotion > neutral, main effect for all events) in each participant.

2.6. Data analysis: laterality measures

Laterality measures were computed using the Lateralisation Index (LI) toolbox in SPM5 (Wilke and Lidzba, 2007), following the basic equation:

$$\frac{\text{Activity (left)} - \text{Activity (right)}}{\text{Activity (left)} + \text{Activity (right)}}$$

with a weighting factor that accounts for asymmetry of masks. The resulting LI therefore ranges from -1 (right lateralised) to 1 (left lateralised) and reflects the distribution of “activated” tissue across hemispheres. For the estimation of activity, the number of supra-threshold voxels (*voxel count*) was used as recommended for large areas of interest (Jansen et al., 2006), with a required minimum of 5 activated voxels on each side (Wilke and Lidzba, 2007). An *adaptive threshold* procedure was employed, using the mean intensity of all voxels in the image as internal threshold under the assumption that relevant responses will be of above-average intensity. There were no significant differences in this internal threshold between the two groups ($p > .30$ for all contrasts). To account for regional differences in residual variance, voxels with high residual variance were de-valued (*variance weighting*). Masks were derived from the parcellation of the MNI brain (Tzourio-Mazoyer et al., 2002). Main analysis involved parietal and temporal cortices, while exploratory analyses were carried out on frontal, occipital cortex, on cortical areas typically involved in language functions (inferior frontal gyrus, superior and middle temporal gyrus, supramarginal, and angular gyrus; Rutten et al., 2002), and the whole brain including deep structures. Hence, statistical testing of our main hypotheses was carried out in a 2 (implicit vs. explicit task instruction) \times 2 (temporal vs. parietal lobe) \times 2 (group) ANCOVA, using a general linear model approach in SPSS, and 2 (implicit vs. explicit task instruction) \times 2 (group) ANCOVA was used for exploratory analyses. Edinburgh Handedness Quotient and emotion identification accuracy (that is, averaged hit rate) were used as covariates. Both variables were mean-centered before entering them into the model. In order to assess the association of lateralisation measures with disorder-related variables (PANSS subscales, CPZ equivalents, time since illness onset, time since first hospitalisation, number of hospitalisations, duration of current hospitalisation) and emotion identification accuracy, those were entered into a multiple regression model in SPSS.

3. Results

3.1. Lateralisation indices: emotional > neutral prosody

Results are shown in Fig. 1 and statistical tests summarised in Table 3. Note that all analyses controlled for emotion identification accuracy differences between the groups. Stronger right lateralisation (or reduced left-lateralisation) to emotional prosody (contrasted with neutral prosody) was observed in the schizophrenia group (compared to the control group). In both groups, right-lateralisation to emotional prosody was stronger in the implicit condition and in the temporal lobe. Less pronounced right-handedness predicted stronger right-lateralisation of BOLD responses to emotional prosody, as indicated by a main effect of handedness. The group difference was found for both tasks and across temporal and parietal lobe (no significant group \times task or group \times lobe interaction).

In a multiple regression with illness-related factors and performance, the PANSS item “affective blunting” emerged as best negative predictor for right-lateralisation in patients with schizophrenia ($R = .66$; $F_{1, 13} = 9.8$; $p < .01$). Patients showed less right-lateralisation when they were more

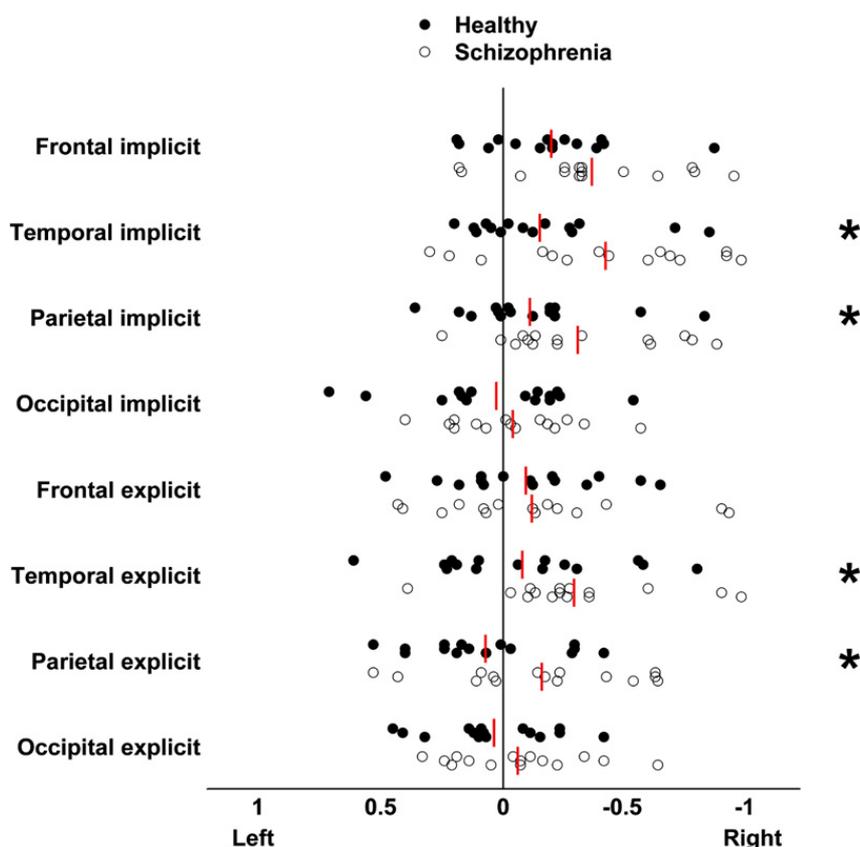


Fig. 1. BOLD responses to emotional as compared with neutral prosody; individual lateralisation indices, ranging from 1 (left) to -1 (right), for healthy individuals (solid dots) and patients with paranoid schizophrenia (outline dots). Group means are depicted as red vertical lines. Significance asterisks refer to *post hoc* *t*-tests that were performed to localise effects, while statistical inference was drawn from ANCOVAs (see results section). * $p < .05$.

affected in their emotional functioning. The only other parameters correlating with right-lateralisation were the PANSS item “poor rapport” ($r = .53$; $p < .05$) and the duration of the current hospitalisation ($r = .54$; $p < .05$), again with patients showing shorter duration of the current treatment or

less poor rapport having stronger right-lateralisation. Lateralisation was not correlated with emotion identification accuracy in the schizophrenia group, and emotion identification accuracy could not explain the effects of the regression analysis. There was no group difference in lateralisation in the frontal lobe and occipital lobe. Stronger right lateralisation was however found in the analysis of language-related areas ($F_{1, 24} = 5.6$; $p < .05$) and across the whole brain ($F_{1, 24} = 7.4$; $p < .05$).

Table 3

Results from the 2 (implicit vs. explicit task instruction) \times 2 (temporal vs. parietal lobe) \times 2 (group) ANCOVA on lateralisation indices with handedness and performance as covariates.

	Emotional > neutral prosody	Prosody > rest
	<i>F</i>	<i>F</i>
Group	9.8***	5.7*
Task	5.2*	4.2(*)
Lobe	10.2***	71.1***
Handedness	7.4*	2.0
Performance	3.1(*)	1.4
Group \times handedness	3.9(*)	6.9*
Group \times handedness \times lobe	2.0	6.4*
Lobe \times handedness	<1	4.7*
Task \times handedness	<1	7.5*
Lobe \times task \times handedness	<1	5.2*
Group \times task \times performance	<1	5.0*
Group difference in temporal lobe	7.0*	7.9**
Group difference in parietal lobe	9.2**	3.7(*)
Group difference in implicit task	7.7*	4.1(*)
Group difference in explicit task	8.0**	7.0*

$df = 1, 24$ for all effects and contrasts. There were no further significant effects. (**) $p < .10$; (*) $p < .05$; ** $p < .01$; *** $p < .005$.

3.2. Lateralisation indices: prosodic speech > baseline

Contrast images for prosodic speech > baseline are shown in Fig. 2 for both groups. Also in this contrast, a stronger right-lateralisation in both lobes and both tasks was observed in patients with schizophrenia (see Fig. 3, Table 3). Both groups had a stronger right-lateralisation in the temporal than in the parietal lobe. Less pronounced right-handedness predicted stronger right-lateralisation in patients with schizophrenia, but not in healthy participants, as shown by the handedness \times group interaction. Further interactions of handedness with other variables are summarised in Table 3.

In a multiple regression model, the PANSS item “affective blunting” again emerged as best negative predictor for right-lateralisation in patients with schizophrenia, i.e. patients with higher values for affective blunting showed less right-lateralisation ($R = .70$; $F_{1, 13} = 12.5$; $p < .005$). The only other parameters correlating with right-lateralisation were the PANSS items “emotional withdrawal” ($r = .53$; $p < .05$) and

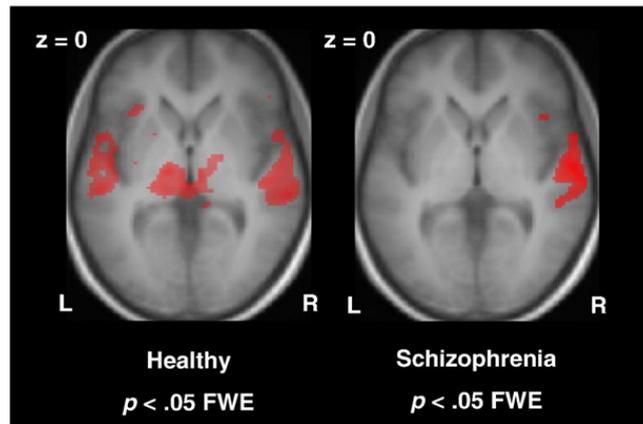


Fig. 2. Group statistical parametric maps (SPMs) of BOLD responses to prosody, as compared to baseline for healthy individuals (left) and patients with schizophrenia (right). Note that statistical analysis relied on individual lateralisation patterns rather than on group SPMs.

“poor rapport” ($r = .54$; $p < .05$). Lateralisation was not correlated with performance in the schizophrenia group, and performance could not explain the results of the regression analysis. There was no group difference in lateralisation in the frontal lobe and occipital lobe. Stronger right lateralisation was also found in analysis of language-related areas ($F_{1, 24} = 6.0$; $p < .05$) and across the whole brain ($F_{1, 24} = 5.7$; $p < .05$).

3.3. Behavioural results

Recognition rates and reaction times for both tasks are summarised in Table 4. Patients with schizophrenia exhibited

less accurate performance ($F_{1, 28} = 8.7$; $p < .01$) and longer reaction times ($F_{1, 28} = 7.1$; $p < .05$) than healthy individuals across both tasks. They were more impaired in recognising emotion categories than recognising gender (interaction task instruction \times group: $F_{1, 28} = 17.1$; $p < .001$), and more impaired when performing on emotional as opposed to neutral prosody (interaction emotion \times group: $F_{2, 28} = 4.0$; $p < .05$). Across both groups, performance in the gender task was higher than in the explicit emotion identification task, ($F_{1, 28} = 141.2$; $p < .001$), performance on neutral items was better than on emotional items ($F_{2, 28} = 30.8$; $p < .001$) and this effect was more pronounced under explicit instructions (interaction

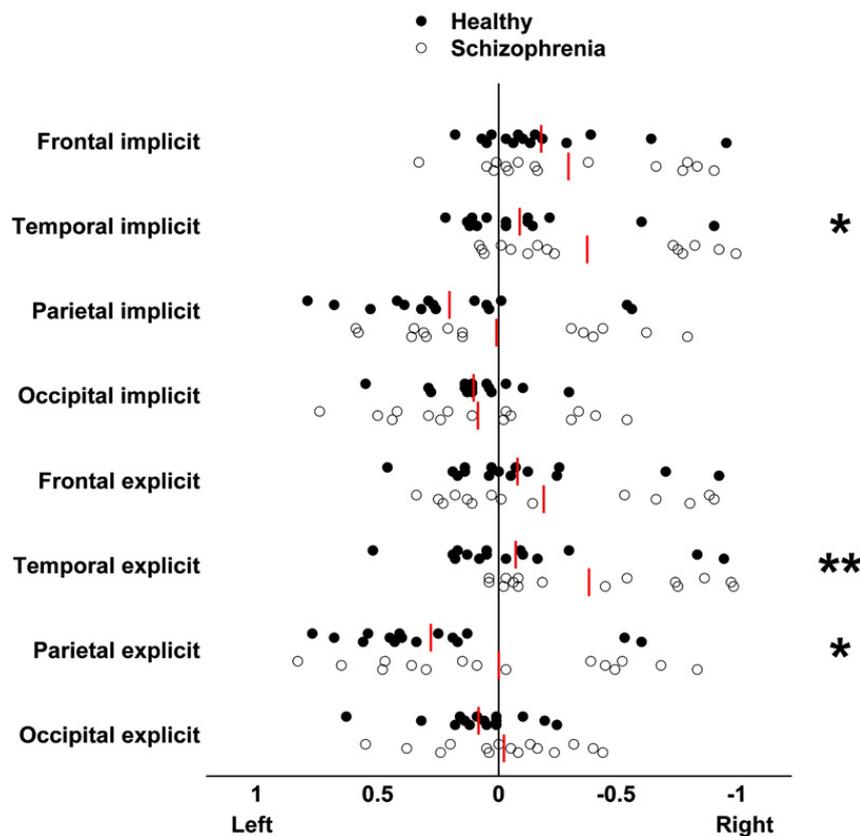


Fig. 3. BOLD responses to prosody, as compared to baseline: individual lateralisation indices, ranging from 1 (left) to -1 (right), for healthy individuals (solid dots) and patients with paranoid schizophrenia (outline dots). Group means are depicted as red vertical lines. Significance asterisks refer to *post hoc* *t*-tests that were performed to localise effects, while statistical inference was drawn from ANCOVAs (see results section). * $p < .05$ ** $p < .01$.

Table 4

Response accuracy (% correct responses) and reaction times (ms) for each stimulus and task type, separated for healthy individuals and patients with schizophrenia.

		Response accuracy (% correct responses)		Reaction times (ms)	
		Gender identification	Emotion identification	Gender identification	Emotion identification
		Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM
Healthy individuals	Neutral	93.3 ± 1.76	81.1 ± 3.54	851 ± 54.0	1530 ± 64.7
	Anger	85.8 ± 1.34	73.9 ± 3.26	901 ± 48.7	1468 ± 96.7
	Fear	86.7 ± 1.9	67.5 ± 2.88	906 ± 55.0	1441 ± 88.2
Patients with schizophrenia	Neutral	94.4 ± 2.13	75.5 ± 6.30	1081 ± 88.9	1724 ± 114.1
	Anger	83.1 ± 1.88	51.7 ± 5.09	1132 ± 87.4	1836 ± 130.6
	Fear	84.7 ± 2.92	45.5 ± 5.43	1132 ± 84.4	1856 ± 129.4

Participants were tasked to identify the speaker's gender for assessment of neural responses associated with implicit appraisal, and to identify the expressed emotion for assessment of neural responses associated with explicit appraisal. All values are mean ± standard error of the mean (SEM).

task instruction × emotion: $F_{2, 28} = 4.4$; $p < .05$). Note that performance differences between groups in identifying emotional prosody was accounted for in analyses of laterality measures by modelling it as covariate.

4. Discussion

The aim of this study was to investigate the lateralisation of cerebral responses to emotional and neutral prosody in patients with paranoid schizophrenia and healthy control participants. Lateralisation indices were calculated that describe a within-subject pattern of cerebral responses and are therefore less likely to be influenced by general alterations in the hemodynamic response due to the disease or psychotropic medication than, for example, a group comparison of statistical parametric maps. As main finding, stronger right-lateralisation (or reduced left-lateralisation) of prosody processing in schizophrenia as compared to healthy control participants was found across both the temporal and parietal lobe and across both implicit and explicit task instructions. This pattern was observed for emotional versus neutral prosody, thus controlling for more general aspects of speech processing, and for all kinds of prosody versus baseline. The same finding emerged when lateralisation indices were calculated for language-related areas, and for the whole brain, however not for the frontal and occipital lobes alone.

4.1. Right lateralisation of emotional processing

Group differences in the contrast between (negative) emotional and neutral prosody can probably not be ascribed to general speech perception processes. Also, effects in this contrast do not reflect prosody processing as such (also neutral prosody is processed) but most likely the detection of (non-neutral) emotions in prosody (Bach et al., 2008a). Increased right-lateralisation in schizophrenia was observed across the temporal and parietal lobe. Exploratory analysis of language-related areas (Rutten et al., 2002), and across the whole brain analysis showed the same results. The differential role of temporal and parietal cortices for various aspects of sound analysis (Bach et al., 2008b; Griffiths and Warren, 2002; Herdener et al., 2007; Mustovic et al., 2003; Pavani et al., 2002) consequently suggests rather unspecific alterations in auditory functions. However, more regionalised alterations cannot be ruled out, since no analysis of smaller regions of interest was undertaken.

4.2. Right lateralisation of prosodic speech processing

Also for the contrast prosodic speech > baseline, stronger right-lateralisation (or reduced left-lateralisation) was found across parietal and temporal lobe, as well as for language related areas and across the whole brain. While this contrast includes the processing aspect of emotional prosody, it is confounded with more general auditory and speech-related functions. A previous study has analysed a similar contrast using an SPM approach and has suggested that cerebral responses prosody in schizophrenia are left-lateralised with a peak in the posterior temporal lobe and temporo-parietal junction (Mitchell et al., 2004). This is incompatible with the consistent finding that patients with schizophrenia show a right-lateralised temporal cortex response to speech, both analysing statistical parametric maps (Ngan et al., 2003; Woodruff et al., 1997) and lateralisation indices (Li et al., 2007; Razafimandimby et al., 2007; Spaniel et al., 2007). Our results – derived from lateralisation indices that are possibly more robust for this purpose than group comparisons of SPMs – are in keeping with these findings and might suggest similar mechanisms underlying lateralisation changes to emotional prosody and to speech in general. Corpus callosum size has recently been linked to lateralisation of speech functions in healthy individuals (Josse et al., 2008), and it appears that corpus callosum is smaller in individuals at risk for psychosis, and further reduced in individuals with chronic schizophrenia (Walterfang et al., 2008a,b). This structure is therefore a possible candidate to explain altered language lateralisation in schizophrenia.

4.3. Impairment in recognizing emotional prosody

There is much evidence that patients with schizophrenia are often impaired in recognising emotions in prosody (see for example Bach et al., in press; Edwards et al., 2001, 2002; Kucharska-Pietura et al., 2005; Leitman et al., 2005). A lesion study has suggested that this dysprosodia resembles right hemispheric lesions (Ross et al., 2001), thus motivating to examine whether a right hemisphere deficit might underlie dysprosodia in schizophrenia. However, although our data on a group level indicate worse performance of patients with schizophrenia in recognising emotional prosody, the performance impairment was not related to the right-lateralisation pattern. This is in line with one study on speech processing in schizophrenia which has reported no association of reduced

left-lateralisation with performance in semantic tasks (Razafimandimby et al., 2007), although an association of the lateralisation changes with more general cognitive functions (Li et al., 2007) and disorganised thinking (Ngan et al., 2003) has been observed.

4.4. Limitations

Limitations of the present study include the small sample size of $N=30$. Also, since no previous study compared explicit and implicit prosody processing in schizophrenia, we included two different task instructions, thus limiting the power to detect overall differences. Our data are confined to the paranoid subtype of schizophrenia as well as to neutral and negative emotional prosody and need further study for generalisation.

4.5. Conclusions

In the present study, we examined the lateralisation of brain responses to negative emotional and neutral prosody during gender identification and emotion recognition. When contrasting patients with schizophrenia to healthy participants, we found an increased right lateralisation (or reduced left-lateralisation) of temporal and parietal responses to emotional as compared to neutral prosody, and to all kinds of prosody compared with baseline. This right-lateralisation was predicted by reduced right-handedness, less pronounced negative symptoms and shorter treatment. Although emotion identification accuracy was reduced in patients, there was no correlation of this deficit with lateralisation. We conclude that the previously found altered lateralisation of speech functions extends to the processing of neutral and emotional prosody in nonsense syllables, possibly with a common underlying dysfunction in language networks.

Role of funding source

DRB was in part supported by the Swiss National Science Foundation, PA00A-117384. The SNSF had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

Contributors

Dominiq R. Bach designed and conducted the experiment, analysed the data and wrote the first draft of the manuscript. Didier Grandjean and David Sander provided stimulus material and helped design the experiment. Erich Seifritz and Werner K. Strik supervised the study. All authors contributed to and have approved the final manuscript.

Conflict of interest

The authors report no conflicts of interest.

Acknowledgements

The authors wish to thank Annick Razafimandimby who helped with data acquisition, and the radiographers team at the Department of Neuroradiology, Inselspital Bern, for their continuing support.

References

- Bach, D.R., Grandjean, D., Sander, D., Herdener, M., Strik, W.K., Seifritz, E., 2008a. The effect of appraisal level on processing of emotional prosody in meaningless speech. *Neuroimage* 42, 919–927.
- Bach, D.R., Schachinger, H., Neuhoff, J.G., Esposito, F., Salle, F.D., Lehmann, C., Herdener, M., Scheffler, K., Seifritz, E., 2008b. Rising sound intensity: an intrinsic warning cue activating the amygdala. *Cereb. Cortex* 18, 145–150.

- Bach, D.R., Buxtorf, K., Grandjean, D., and Strik, W.K., in press. The influence of emotion clarity on emotional prosody identification in paranoid schizophrenia. *Psychol. Med.*
- Banse, R., Scherer, K.R., 1996. Acoustic profiles in vocal emotion expression. *J. Pers. Soc. Psychol.* 70, 614–636.
- Devlin, J.T., Raley, J., Tunbridge, E., Lanary, K., Floyer-Lea, A., Narain, C., Cohen, L., Behrens, T., Jezzard, P., Matthews, P.M., Moore, D.R., 2003. Functional asymmetry for auditory processing in human primary auditory cortex. *J. Neurosci.* 23, 11516–11522.
- Edwards, J., Pattison, P.E., Jackson, H.J., Pattison, P.E., Wales, R.J., 2001. Facial affect and affective prosody recognition in first-episode schizophrenia. *Schizophr. Res.* 48, 235–253.
- Edwards, J., Jackson, H.J., Pattison, P.E., 2002. Emotion recognition via facial expression and affective prosody in schizophrenia: a methodological review. *Clin. Psychol. Rev.* 22, 789–832.
- Grandjean, D., Banziger, T., Scherer, K.R., 2006. Intonation as an interface between language and affect. *Prog. Brain Res.* 156, 235–247.
- Griffiths, T.D., Warren, J.D., 2002. The planum temporale as a computational hub. *Trends Neurosci.* 25, 348–353.
- Herdener, M., Esposito, F., Di Salle, F., Lehmann, C., Bach, D.R., Scheffler, K., Seifritz, E., 2007. BOLD correlates of edge detection in human auditory cortex. *Neuroimage* 36, 194–201.
- Jansen, A., Menke, R., Sommer, J., Forster, A.F., Bruchmann, S., Hempleman, J., Weber, B., Knecht, S., 2006. The assessment of hemispheric lateralization in functional MRI-robustness and reproducibility. *Neuroimage* 33, 204–217.
- Josse, G., Seghier, M.L., Kherif, F., Price, C.J., 2008. Explaining function with anatomy: language lateralization and corpus callosum size. *J. Neurosci.* 28, 14132–14139.
- Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr. Bull.* 13, 261–276.
- Kucharska-Pietura, K., David, A.S., Masiak, M., Phillips, M.L., 2005. Perception of facial and vocal affect by people with schizophrenia in early and late stages of illness. *Br. J. Psychiatry* 187, 523–528.
- Leitman, D.L., Foxe, J.J., Butler, P.D., Saperstein, A., Revheim, N., Javitt, D.C., 2005. Sensory contributions to impaired prosodic processing in schizophrenia. *Biol. Psychiatry* 58, 56–61.
- Li, X., Branch, C.A., Ardekani, B.A., Bertisch, H., Hicks, C., DeLisi, L.E., 2007. fMRI study of language activation in schizophrenia, schizoaffective disorder and in individuals genetically at high risk. *Schizophr. Res.* 96, 14–24.
- Mitchell, R.L.C., Elliott, R., Barry, M., Cruttenden, A., Woodruff, P.W.R., 2004. Neural response to emotional prosody in schizophrenia and in bipolar affective disorder. *Br. J. Psychiatry* 184, 223–230.
- Mustovic, H., Scheffler, K., Di Salle, F., Esposito, F., Neuhoff, J.G., Hennig, J., Seifritz, E., 2003. Temporal integration of sequential auditory events: silent period in sound pattern activates human planum temporale. *Neuroimage* 20, 429–434.
- Ngan, E.T., Vouloumanos, A., Cairo, T.A., Laurens, K.R., Bates, A.T., Anderson, C.M., Werker, J.F., Liddle, P.F., 2003. Abnormal processing of speech during oddball target detection in schizophrenia. *Neuroimage* 20, 889–897.
- Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9, 97–113.
- Pavani, F., Macaluso, E., Warren, J.D., Driver, J., Griffiths, T.D., 2002. A common cortical substrate activated by horizontal and vertical sound movement in the human brain. *Curr. Biol.* 12, 1584–1590.
- Razafimandimby, A., Maiza, O., Herve, P.Y., Lecardeur, L., Delamillieure, P., Brazo, P., Mazoyer, B., Tzourio-Mazoyer, N., Dollfus, S., 2007. Stability of functional language lateralization over time in schizophrenia patients. *Schizophr. Res.* 94, 197–206.
- Ross, E.D., Orbelo, D.M., Cartwright, J., Hansel, S., Burgard, M., Testa, J.A., Buck, R., 2001. Affective-prosodic deficits in schizophrenia: comparison to patients with brain damage and relation to schizophrenic symptoms [corrected]. *J. Neurol. Neurosurg. Psychiatry* 70, 597–604.
- Rutten, G.J., Ramsey, N.F., van Rijen, P.C., van Veelen, C.W., 2002. Reproducibility of fMRI-determined language lateralization in individual subjects. *Brain Lang.* 80, 421–437.
- Scherer, K.R., 2005. Feelings integrate the central representation of appraisal-driven response organization in emotion. In: Manstead, A.S.R., Frijda, N.H., Fischer, A.H. (Eds.), *Feelings and Emotions: The Amsterdam Symposium*. Cambridge University Press, Cambridge, pp. 136–157.
- Sommer, I., Ramsey, N., Kahn, R., Aleman, A., Bouma, A., 2001. Handedness, language lateralisation and anatomical asymmetry in schizophrenia: meta-analysis. *Br. J. Psychiatry* 178, 344–351.
- Spaniel, F., Tintera, J., Hajek, T., Horacek, J., Dezortova, M., Hajek, M., Dockery, C., Kozeny, J., Hoschl, C., 2007. Language lateralization in monozygotic twins discordant and concordant for schizophrenia. A functional MRI pilot study. *Eur. Psychiatry* 22, 319–322.
- Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., Joliot, M., 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage* 15, 273–289.

- Walterfang, M., Wood, A.G., Reutens, D.C., Wood, S.J., Chen, J., Velakoulis, D., McGorry, P.D., Pantelis, C., 2008a. Morphology of the corpus callosum at different stages of schizophrenia: cross-sectional study in first-episode and chronic illness. *Br. J. Psychiatry* 192, 429–434.
- Walterfang, M., Yung, A., Wood, A.G., Reutens, D.C., Phillips, L., Wood, S.J., Chen, J., Velakoulis, D., McGorry, P.D., Pantelis, C., 2008b. Corpus callosum shape alterations in individuals prior to the onset of psychosis. *Schizophr. Res.* 103, 1–10.
- WHO, 2004. International statistical classification of diseases and health related problems (Tenth revision) ICD-10. World Health Organisation, Geneva.
- Wilke, M., Lidzba, K., 2007. LI-tool: a new toolbox to assess lateralization in functional MR-data. *J. Neurosci. Methods* 163, 128–136.
- Woodruff, P.W., Wright, I.C., Bullmore, E.T., Brammer, M., Howard, R.J., Williams, S.C., Shapleske, J., Rossell, S., David, A.S., McGuire, P.K., Murray, R.M., 1997. Auditory hallucinations and the temporal cortical response to speech in schizophrenia: a functional magnetic resonance imaging study. *Am. J. Psychiatry* 154, 1676–1682.