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Altered attentional processing of happy prosody in schizophrenia

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ABSTRACT

Background: Abnormalities in emotional prosody processing have been consistently reported in schizophrenia. Emotionally salient changes in vocal expressions attract attention in social interactions. However, it remains to be clarified how attention and emotion interact during voice processing in schizophrenia. The current study addressed this question by examining the P3b event-related potential (ERP) component.
Method: The P3b was elicited with a modified oddball task, in which frequent ($p = .84$) neutral stimuli were intermixed with infrequent ($p = .16$) task-relevant emotional (happy or angry) targets. Prosodic speech was presented in two conditions - with intelligible (semantic content condition - SCC) or unintelligible semantic content (prosody-only condition - POC). Fifteen chronic schizophrenia patients and 15 healthy controls were instructed to silently count the target vocal sounds.
Results: Compared to controls, P3b amplitude was specifically reduced for happy prosodic stimuli in schizophrenia, irrespective of semantic status. Groups did not differ in the processing of neutral standards or angry targets.
Discussion: The selectively reduced P3b for happy prosody in schizophrenia suggests top-down attentional resources were less strongly engaged by positive relative to negative prosody, reflecting alterations in the evaluation of the emotional salience of the voice. These results highlight the role played by higher-order processes in emotional prosody dysfunction in schizophrenia.

1. Introduction

Abnormalities in the perception and recognition of emotional prosody have been increasingly recognized as a core feature of schizophrenia (Couture et al., 2006). Deficits in emotional perception seem to be independent of antipsychotic medication and to represent a trait deficit (Edwards et al., 2001; Kucharska-Pietura et al., 2005). Further, they predict functional outcome and quality of life (Kee et al., 2003). Emotional prosody, the non-verbal vocal expression of emotion (Kotz and Paulmann, 2011), is a cornerstone of adaptive functioning in a social environment (Schirmer and Kotz, 2006). At perceptual and physical levels, vocal emotions are primarily communicated by means of pitch (fundamental frequency – F0), intensity and duration (e.g., duration of syllables and pauses) (Banse and Scherer, 1996; Juslin and Laukka, 2003). Perceiving the emotional quality of the voice is a multi-stage process that includes: 1) decoding the acoustic properties of the voice; 2) detecting emotionally salient acoustic cues; and 3) cognitively evaluating the emotional significance of the voice (Paulmann et al., 2010; Paulmann and Kotz, 2008a, 2008b; Pinheiro et al., 2014, 2013; Wildgruber et al., 2006).

Relative to the study of facial affect processing, fewer studies have examined emotional prosody dysfunction in schizophrenia. The existing studies revealed alterations in emotional prosody processing in schizophrenia using behavioral (Edwards et al., 2001; Kucharska-Pietura et al., 2005; Leitman et al., 2010a; Pawełczyk et al., 2018; Shaw et al., 1999; Shea et al., 2007; Vaskinn et al., 2007), functional magnetic resonance imaging (fMRI – Leitman et al., 2011; Mitchell et al., 2004), and event-related potential (ERP – Kantrowitz et al., 2015; Leitman et al., 2010b; Pinheiro et al., 2014, 2013) measures. Impaired recognition of emotion from a tone of a voice (e.g., Dondaine et al., 2014) may lead to dysfunctional social interactions (e.g., Hooker and Park, 2002) and contribute to positive symptoms such as auditory verbal hallucinations (Alba-Ferrara et al., 2012; Shea et al., 2007). There is some evidence that impairments in emotional vocal recognition in schizophrenia are enhanced when stimuli have a negative valence (Bozikas et al., 2006; Edwards et al., 2001; Huang et al., 2009; Ito et al., 2013; Pinheiro et al., 2013), even though other studies found worse performance in the recognition of more complex vocal stimuli with a positive valence such as alluring voices (Vogel et al., 2016). Notwithstanding, alterations in ERP responses of the electroencephalogram to vocal emotional information occurring before a response is made (i.e., deciding whether the voice

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is happy or angry, for example) were observed irrespective of valence (Pinheiro et al., 2014) Pinheiro et al., 2013.

More recent findings suggest a faulty interaction between sensory-based and higher-order neural systems as contributing to abnormal emotional prosody processing in schizophrenia (Kantrowitz et al., 2015; Leitman et al., 2010b; Pinheiro et al., 2014, 2013). ERP studies are particularly useful to shed light on the timing of the processes underlying emotional decoding from a set of auditory cues. These studies revealed differences between schizophrenia patients and healthy controls in the N1 and P2 components, which depended on stimulus complexity (Pinheiro et al., 2013, 2014). Schizophrenia patients showed reduced N1 amplitude in response to neutral and emotional sentences (Pinheiro et al., 2013) and single words (Pinheiro et al., 2014) with intelligible semantic content. P2 modulations were observed as a function of valence and semantic status: the P2 was increased in response to both angry and happy sentences with intelligible semantic content and to happy prosodic pseudosentences (Pinheiro et al., 2013), whereas it was selectively increased in response to happy words with intelligible semantic content (Pinheiro et al., 2014). These findings revealed alterations in sensory processing (N1) and valence-specific alterations in the integration of emotionally significant acoustic cues (P2) in schizophrenia, which were enhanced when the speech signal contained intelligible semantic information presented in sentence format. These early alterations (~200 ms post-stimulus onset) may in turn affect processes related to emotional change detection in the voice.

While it is well established that emotional prosody processing abnormalities are present in schizophrenia, the specific contributions of higher-order cognitive impairments to altered processing of vocal emotions are not yet fully understood. An example of a critical higher-order cognitive process involved in emotional prosody perception in general, and emotional change detection in particular, is selective attention. In social interactions, emotionally relevant cues (e.g., a change of voice from neutral to angry) may selectively capture attention, ensuring that processing resources are oriented toward events with high salience (Pinheiro et al., 2015a, 2015b). There is a robust body of evidence indicating that attention may change the processing of vocal emotions, leading to the top-down prioritization of certain stimulus features (Frühholz and Grandjean, 2013; Pinheiro et al., 2017a, 2017b; Sander et al., 2005). For example, activation of the amygdala was observed only when the task involved directing attention toward the vocal expressions (Frühholz et al., 2012).

ERP studies have revealed effects of selective attention approximately at 300 ms post-stimulus onset as reflected in the P300. The P300 ERP component is a neurophysiological index of attentional resources allocation during stimulus processing (Polich, 2007). In the classical oddball paradigm, a low-probability stimulus (target) is embedded in a series of frequent or task-irrelevant stimuli and needs to be detected (Ford, 1999; Polich, 2007). The P300 is composed of dissociable components (Spencer et al., 2001, 1999): whereas the fronto-central P3a is elicited by rare or novel task-irrelevant stimuli and reflects stimulus-driven attention orienting (e.g., Courchesne et al., 1975), the centro-parietal P3b is elicited by infrequent task-relevant stimuli (e.g., Polich, 2007; Sutton et al., 1965). Therefore, the P3b is considered an important signature of late cognitive functions (Linden, 2005): it reflects the top-down allocation of attentional resources (Polich, 2007) for subsequent update of a mental model of the environment in memory (Polich, 2007). Critically, the P300 is sensitive to the emotional salience of the stimulus: studies using emotional stimuli have demonstrated that emotional vocal cues grab more attention than neutral cues (P3a – Pinheiro et al., 2015a; Thierry and Roberts, 2007; P3b – Campanella et al., 2010; Pinheiro et al., 2017a); some have revealed valence-related differences in P300 amplitude such as increased P3b for positive compared to negative vocal cues (Pinheiro et al., 2017a).

Reduced P3a (e.g., Atkinson et al., 2012; Cortiñas et al., 2008; Kaur et al., 2011; Nagai et al., 2013; Takahashi et al., 2013) and P3b (e.g., McCarley et al., 1993; Potts et al., 1998) amplitude to stimuli signaling a change in the environment is a consistent finding in schizophrenia and was identified as a potential marker of the schizophrenia prodrome (reviewed in Ford, 1999). P300 abnormalities are present in off-medication schizophrenia individuals, first-episode schizophrenia and never-medicated schizotypal participants, but not in bipolar manic patients (Turetsky et al., 2007). P300 abnormalities may therefore reflect limited attentional resources available or allocated to the task (Ford, 1999) or a deficit in updating a model of the environment or context (Spencer et al., 2001; Turetsky et al., 2007).

Prior studies with prosodic stimuli have not explicitly addressed the role of top-down attention-dependent processes in altered decoding of emotions from the voice. Attention bias mechanisms may impact upon the processing of emotionally salient information in social contexts in a valence-dependent manner. Specifically, disrupted selective attention may contribute to the observed emotional prosody recognition impairments in schizophrenia.

1.1. The current study and hypotheses

The ability to detect emotional changes in the voice in everyday communication is critical for effective functioning in social situations. This study examined how emotion and selective attention interact in voice processing in schizophrenia. We used a modified oddball task, in which frequent (standard) neutral prosodic stimuli were intermixed with infrequent task-relevant (target) emotional prosodic stimuli differing in valence (negative [anger] vs. positive [happiness]). Extending our prior work (Pinheiro et al., 2014, 2013), prosodic stimuli with intelligible (semantic content condition - SCC) and unintelligible semantic content (prosody-only condition - POC) were contrasted to examine the role of semantic cues in emotional prosody change detection. As the P3b taps into later, elaborative stages of processing, it is particularly suited to examine the contribution of attention bias mechanisms to altered decoding of vocal emotions.

We hypothesized abnormalities in the allocation of attention to emotional vocal changes in schizophrenia, reflected in reduced P3b amplitude, which was expected to be modulated by stimulus valence. Consistent with previous studies with single words (where abnormal P2 was found to happy but not angry prosody [Pinheiro et al., 2014], suggesting a specific impairment in categorizing happy auditory emotional percepts as "salient"), we expected larger P3b deficits in response to prosodic stimuli with positive valence (happy prosody) than with negative valence. In addition, considering prior evidence demonstrating that concurrently available semantic information in the speech signal contributes to emotional prosody processing abnormalities in schizophrenia (Pinheiro et al., 2014, 2013), we hypothesized that P3b abnormalities would be enhanced when the voice carried intelligible (SCC) compared to unintelligible semantic content (POC).

2. Methods

2.1. Participants

Fifteen patients with a diagnosis of chronic schizophrenia (American Psychiatric Association, 2000) and 15 healthy comparison individuals (HC) participated in this study. Patients were recruited at the Veterans Affairs (VA) Administration Hospital – Brockton, MA, from inpatient and outpatient units. Comparison subjects were recruited from advertisements in local newspapers and the internet. The inclusion criteria were: English as first language; right handedness (Oldfield, 1971); no history of neurological illness; no DSM-IV diagnosis of drug or alcohol abuse (American Psychiatric Association, 2000) in the last five years; verbal intelligence quotient (IQ) above 85 (Wechsler, 1997); no hearing, vision or upper body impairment.

Control participants were matched to patients on the basis of age, gender and parental socio-economic status (Hollingshead, 1975). For HC, additional inclusion criteria were: no history of Axis I or II disorders as determined by the SCID for Axis I (SCID-I; First et al., 2002) and Axis II (SCID-II; First et al., 1997) disorders; no history of Axis I disorder in first or second degree family members, determined by the Family History-Research Diagnostic Criteria instrument (Andreasen et al., 1977).

Patients were diagnosed (screened for HC) using SCID-I (First et al., 2002) and SCID-II (First et al., 1997). Symptom severity was assessed with the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987), the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983) and the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984) (Table 1).

Before participation in the study, all participants had the procedures fully explained to them and read and signed an informed consent form to confirm their willingness to participate in the study (following Harvard Medical School and Veterans Affairs Boston Healthcare System guidelines). Participants were paid $15 per hour for voluntary completion of the study.

2.2. Stimuli

Stimuli consisted of the word “body” uttered by a female speaker of American English, with training in theatre techniques, with neutral, happy and angry prosody. The word was chosen because of its neutral semantic content (Bradley and Lang, 1999) and short length. The word was recorded with happy, angry and neutral prosody, in a quiet room with an Edirol R-09 recorder and a CS-15 cardioid-type stereo microphone, with a sampling rate of 22 kHz and 16-bit quantization. The word ‘body’ was spoken several times with neutral, happy and angry prosody to allow the selection of the best exemplar of each prosody type. The emotional category of the different exemplars of the word ‘body’ was subsequently assessed by a group of individuals (n = 15) not participating in the ERP experiment. The three prosody type exemplars that were assessed by at least 99% of participants as having “happy”, “angry”, or “neutral” intonation were selected for the experiment. Anger and happiness were selected as they have similar acoustic profiles, such as high intensity and variable F0 (e.g., Banse and Scherer, 1996), and represent emotional categories that regularly occur in social contexts. Auditory stimuli were acoustically analyzed using Praat (Boersma and Weenink, 2013; Table 2).

Two versions of the task were presented: 1) in the SCC, the semantic content of the prosodic words was intelligible; 2) in the POC, the semantic content of the prosodic words was unintelligible after acoustic transformation based on Ramus and Mehler (1999; Fig. 1). In order to ensure that stimuli in the POC condition were indeed devoid of semantic content, 10 volunteers (who did not participate in the ERP experiment) listened to the stimuli and were asked to indicate whether the speech sounds they have heard had an intelligible meaning, i.e. whether it existed in the English language. If they responded ‘yes’, they were additionally instructed to indicate which word have they listened to. All participants responded that the speech sounds had no intelligible meaning.

An additional group of participants (n = 28) evaluated the valence and arousal of both SCC and POC words using the Self-Assessment Manikin (Bradley and Lang, 1994). Emotion category was found to affect valence ratings ($F(2, 54) = 77.572$, $p < .001$, $\eta_p^2 = 0.742$): happy stimuli were rated as more positive compared to both angry ($p < .001$) and neutral ($p < .001$) stimuli; angry stimuli were rated as more negative compared to both happy ($p < .001$) and neutral ($p < .001$) stimuli ($\text{Valence}_{\text{Happy}}$: M ± SD = 6.43 ± 1.06; $\text{Valence}_{\text{Neutral}}$: 5.14 ± 1.35; $\text{Valence}_{\text{Angry}}$: 3.04 ± 1.19). An effect of semantic status ($F(1, 27) = 6.000$, $p = .021$, $\eta_p^2 = 0.182$) revealed generally more positive valence ratings in the SCC (M ± SD = 5.04 ± 1.22) compared to the POC condition (M ± SD = 4.70 ± 1.17). Emotion category also modulated arousal ratings ($F(2, 54) = 10.001$, $p < .001$, $\eta_p^2 = 0.270$): both angry and happy stimuli were rated as more arousing compared to neutral stimuli (angry > neutral - $p = .014$; happy > neutral – $p < .001$), but perceived arousal did not differ between angry and happy stimuli ($p > .05$; $\text{Arousal}_{\text{Angry}}$: M ± SD = 4.50 ± 2.28; $\text{Arousal}_{\text{Happy}}$: M ± SD = 4.93 ± 1.77; $\text{Arousal}_{\text{Neutral}}$: M ± SD = 3.32 ± 1.74;). Further, arousal ratings were not affected by the semantic status of the speech stimuli ($F(1, 27) = 0.090$, $p = .766$).

2.3. Procedure

Each participant was seated comfortably at a distance of 100 cm from a computer monitor in a sound-attenuating chamber. The two versions of the task were presented in a counterbalanced way. Each condition – SCC and POC – consisted of 2 blocks (block 1: neutral standards and happy targets; block 2: neutral standards and angry targets). Each block included 170 standards ($p = .84$) and 32 target sounds ($p = .16$). This number was determined after a pilot study that aimed to verify the feasibility of the experimental protocol in eliciting the P3b component while minimizing fatigue and, simultaneously, maximizing attention to the sounds. Considering the consistently reported

Table 1
Demographic, cognitive and clinical characteristics of participants.

Variable	Healthy controls (n = 15)	Schizophrenia patients (n = 15)	*t*, *p* value[b]
Age (years)	44.21 (5.78)	42.36 (9.15)	0.642, 0.427
Women, n	5	4	
Education (years)	15.27 (1.67)	13.47 (2.23)	2.502, 0.018[*]
Subject's SES[a]	2.20 (0.78)	3.29 (1.33)	−2.715, 0.011[*]
Parental SES	2.40 (0.83)	2.64 (1.39)	−0.576, 0.570
Cognitive data			
Verbal comprehension index	99.08 (11.47)	92.64 (13.03)	1.327, 0.197
Full scale IQ	99.33 (12.30)	90.43 (13.34)	1.758, 0.091
Clinical data			
Illness duration (years)	NA	14.22 (8.48)	NA
Chlorpromazine EQ(mg)	NA	445.79 (327.44)	NA
PANSS delusions	NA	5.31 (2.06)	NA
PANSS conceptual disorganization	NA	2.62 (1.12)	NA
PANSS hallucinations	NA	4.92 (1.89)	NA
PANSS positive scale	NA	23.54 (7.62)	NA
PANSS negative scale	NA	22.69 (10.15)	NA
PANSS general psychopathology	NA	44.08 (15.72)	NA
PANSS total psychopathology	NA	90.31 (29.41)	NA
SANS total	NA	11.77 (6.91)	NA
SAPS total	NA	10.38 (2.84)	NA

Notes. All values represent mean ± SD. SES = socioeconomic status; Chlorpromazine EQ = Chlorpromazine Equivalent Dose; NA = not applicable.
[a] Hollingshead Four-Factor Index of Social Status (Hollingshead, 1975).
[b] Independent sample *t*-tests tested for group differences in age, SES, parental SES, and IQ.
[*] $p < .05$.

Table 2
Acoustic properties of neutral, happy, and angry prosody in the semantic content (SCC) and prosody-only (POC) conditions.

Semantic status	Emotion	Acoustic properties						
		Duration (ms)	F0 (Hz)			Intensity (dB)		
			Minimum	Mean	Maximum	Minimum	Mean	Maximum
SCC	Angry	600	233.00	253.75	282.25	67.00	74.67	78.33
	Happy	600	318.75	347.00	391.50	77.33	81.67	84.33
	Neutral	600	152.33	166.33	184.67	60.50	72.25	75.75
POC	Angry	600	224.50	250.50	273.50	71.25	78.00	81.00
	Happy	600	303.67	339.33	375.33	71.00	77.50	80.25
	Neutral	600	199.25	201.50	203.75	67.25	77.75	80.75

Note. Numbers represent means.

attentional deficits in schizophrenia (reviewed in Ford, 1999), and to ensure that the conditions mentioned above were kept, only four blocks were included in the final protocol.

Stimuli were delivered binaurally over headphones. Before word onset, a fixation cross was presented centrally on the screen for 1000 ms and remained there during auditory word presentation to minimize eye movements. The inter-stimulus interval (ISI) was jittered 800–1200 ms. The order of blocks was counterbalanced across participants. In each block, participants were asked to silently count the number of targets. The task lasted approximately 60 min.

2.4. EEG data acquisition and analysis

During the task, the EEG was recorded using a 64-channel BioSemi Active 2 system and a custom-designed electrode cap (Electro-cap International). EEG was acquired in a continuous mode at a digitization rate of 512 Hz, and stored on hard disk for later analysis. Horizontal and vertical electrooculograms (EOG) were recorded for eye movement and blink detection and rejection, via electrodes placed on the left and right temples and one below the left eye. During data acquisition, the activity in all channels was referred to the system's internal loop (CMS/DRL sensors).

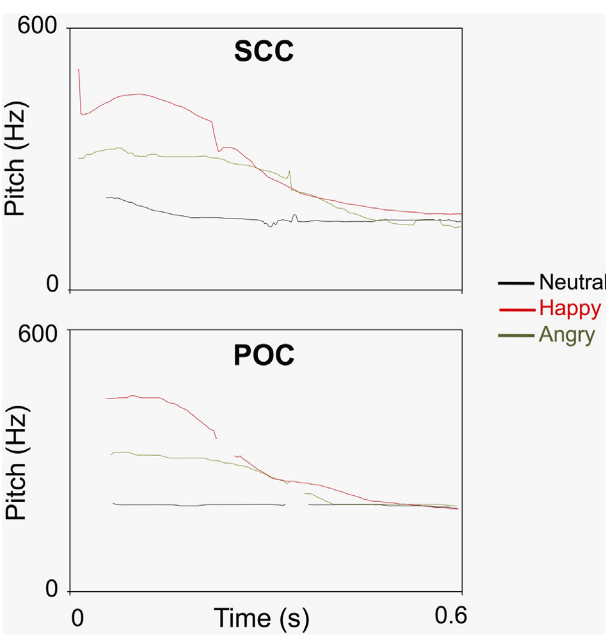

Fig. 1. Pitch contour of speech signals before (SSC) and after (POC) concatenative synthesis, for each of the prosody types (happy, angry, and neutral). *Note.* Based on procedures of Ramus and Mehler (1999), duration and f0 values were transferred to MBROLA (Dutoit et al., 1996) for concatenative synthesis by using the American English (female) diphone database, ensuring that the synthesis of new words preserved characteristics such as global intonation, syllabic rhythm and broad phonotactics (Ramus and Mehler, 1999). This technique eliminates intelligible lexical–semantic content while preserving emotional prosody (Pinheiro et al., 2013, 2014).

The EEG data were processed using Brain Vision Analyzer 2 software (Brain Products GmbH, Germany). Data were referenced offline to the average of the left and right mastoids and high-pass filtered with a 0.1 Hz filter. Individual ERP epochs for each condition were created using a 200 ms pre-stimulus baseline and 800 ms post-stimulus epoch to standard (neutral) prosodic stimuli, and to the two target types: happy prosody and angry prosody. The EEG signal was corrected using the −200 to 0 ms pre-stimulus interval as baseline. Ocular artifacts were corrected using the algorithm of Gratton et al. (1983). Segments were also semiautomatically screened for eye movements, muscle artifacts, electrode drifting and amplifier blocking. EEG epochs containing eye blinks or movement artifacts exceeding ±100 microvolts were not included in individual ERP averages. After artifact rejection, at least 80% of trials per condition per subject entered the analyses. The number of individual trials did not differ between groups ($p > .05$).

Based on visual inspection of the ERP waveforms and on prior studies (e.g., Onitsuka et al., 2013), P3b was analyzed as mean amplitude in the 300–500 ms latency window, at Fz, F3, F4 (frontal ROI), Cz, C3, C4 (central ROI), Pz, P3, P4 (parietal ROI). Mean amplitude in this interval was analyzed separately for standard and target vocal sounds to understand whether diagnosis affected the processing of expected and unexpected stimuli in the same manner. Grand average waveforms are shown in Figs. 2 and 3.

2.5. Statistical analyses

2.5.1. P3b

P3b amplitude was analyzed with mixed linear models using the lmer4 (Bates et al., 2015) and lmerTest (Kuznetsova et al., 2016) packages in the R environment (R3.4.3. GUI 1.70), which were used to estimate fixed and random coefficients. In contrast to the more traditional repeated-measures ANOVA analysis, LMER allows controlling for the variance associated with random factors such as random effects for participants in ERP amplitude (Baayen et al., 2008).

Intra-class correlation coefficients indicated that 43.5% of the total variance in the P3b response was accounted for by differences between participants. A Gaussian distribution of residuals was selected to run the mixed model and probability plots (quantile-quantile plots) confirmed its adequacy. P3b amplitude was included as outcome, participants were included as random effects, whereas semantic status (SCC, POC), emotion (happy, angry), ROI (frontal, central, parietal), and group were included as fixed effects.

2.5.2. Relationship between P3b and clinical data

Spearman's Rho correlations were performed in an exploratory analysis of the relationship between ERP amplitude for happy and angry targets (at Fz, Cz and Pz) in both SSC and POC conditions, and clinical scales (PANSS; SANS; SAPS). Based on prior studies, we were especially interested in testing the relationship between P3b and positive symptoms, particularly hallucinations (Alba-Ferrara et al., 2012; Shea et al., 2007).

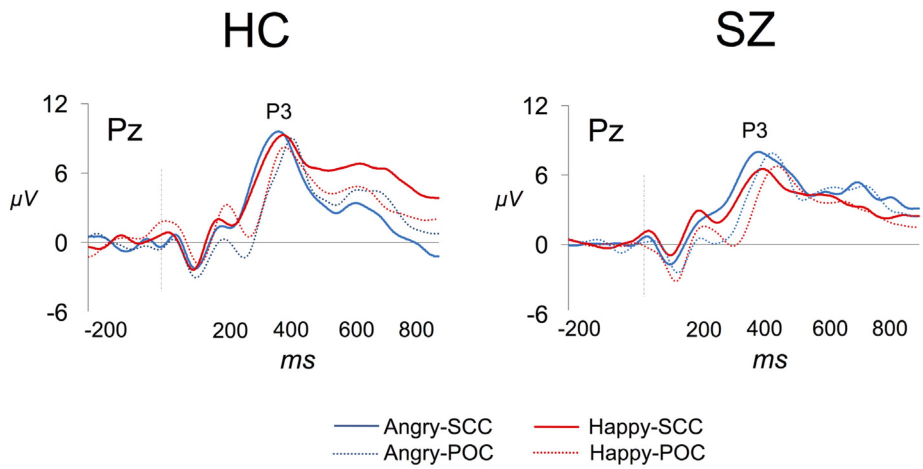

Fig. 2. Grand average waveforms for angry and happy targets in the semantic content (SCC) and prosody-only (POC) conditions, in both healthy controls (HC) and schizophrenia patients (SZ) at Pz electrode.

In addition, we correlated P3b amplitude with mean equivalent chlorpromazine (CPZ) dosage, as well as with illness duration to test for effects of medication and chronicity. All significance levels are two-tailed with pre-set significance alpha level of $p < .05$.

3. Results

3.1. Behavioral data

Groups did not differ in the number of targets counted across emotion types and semantic status conditions ($p > .05$; HC $= 30.78 \pm 1.88$; SZ $= 30.52 \pm 2.83$).

3.2. P3b

3.2.1. Processing of standards

Amplitude was more positive in response to frequent POC speech compared to frequent SCC speech (semantic status – $\beta = 1.321$, SE $=$ 0.479, $t(330) = 2.756$, $p = .006$). Group did not affect the ERP response to standards ($\beta = -0.515$, SE $= 0.618$, $t(131) = -0.834$, $p = .406$).

3.2.2. Processing of targets

Semantic status affected the P3b amplitude ($\beta = -1.449$, SE $=$ 0.339, $t(330) = -4.277$, $p < .001$): prosodic speech with unintelligible semantic content (POC) resulted in reduced P3b amplitude compared

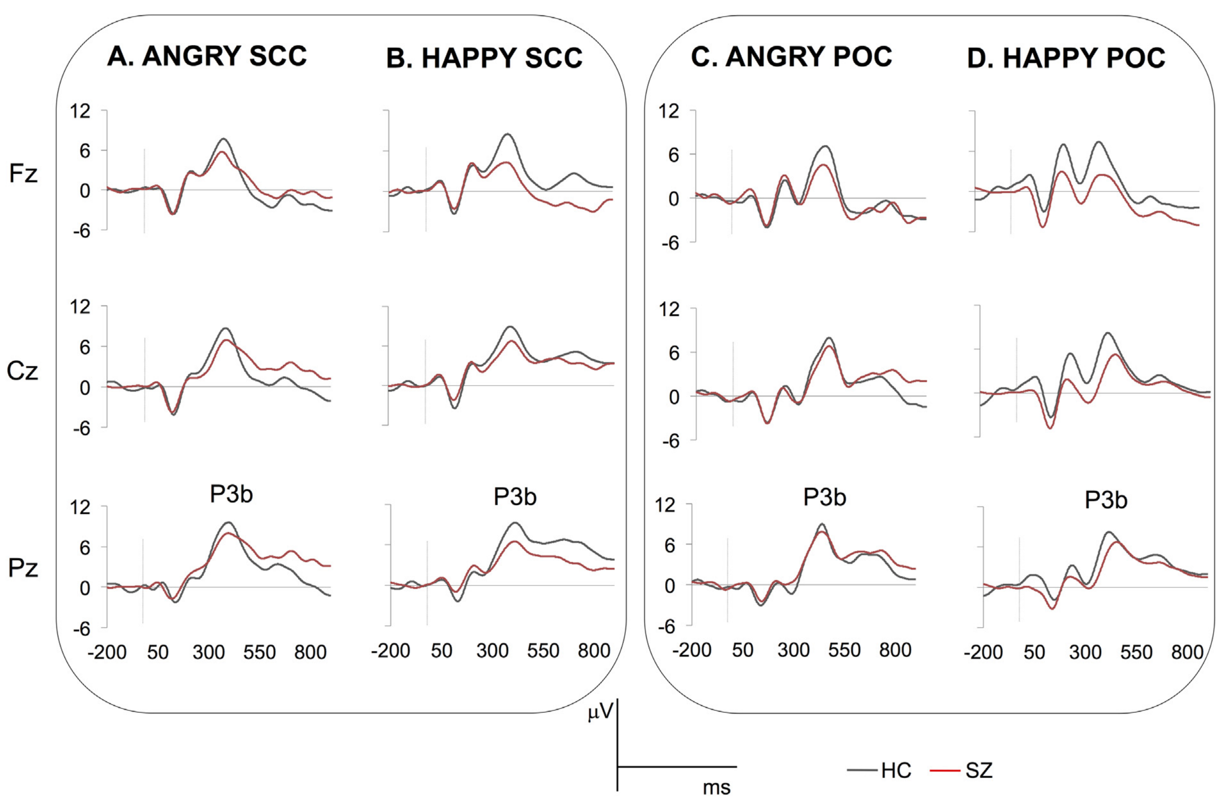

Fig. 3. Grand average waveforms illustrating group comparisons for angry and happy targets in the semantic content (SCC) and prosody-only (POC) conditions at Fz, Cz and Pz electrodes.

to SCC prosodic speech. As expected, P3b amplitude was more positive at parietal electrodes compared to frontal ones (β = 2.240, SE = 0.391, $t(330) = 5.733$, $p < .001$), and at central electrodes compared to frontal ones (β = 1.552, SE = 0.391, $t(330) = 3.972$, $p < .001$).

Importantly, group interacted with emotion but not with semantic status (β = −1.662, SE = 0.640, $t(330) = -2.597$, $p = .010$): happy prosodic speech, irrespective of semantic status, elicited smaller (less positive) P3b amplitude in schizophrenia patients compared to healthy controls (β = −2.2086, SE = 1.0271, $t(30) = -2.159$, $p = .040$); P3b amplitude in response to angry prosodic speech was similar in both groups (β = −0.5466, SE = 1.3178, $t(30) = -0.415$, $p = .681$).

To account for the role of the acoustic properties of the stimuli, mean F0 and mean intensity of the voice stimuli were included as fixed factors in the statistical model. None of the factors had a significant effect on P3b amplitude (mean F0 – β = −0.1059, SE = 0.1447, $t(330) = -0.732$, $p = .465$; mean intensity – β = −0.0624, SE = 0.0894, $t(330) = -0.698$, $p = .486$).

3.3. Correlations between P3b and clinical data

No significant correlation was found between P3b amplitude, clinical data, CPZ equivalent or illness duration ($p > .05$).

4. Discussion

The perception of vocal emotional information is a complex process that relies on the analysis of modality-dependent sensory information and on modality-independent cognitive operations in which emotional meaning is derived from sensory data (Frühholz et al., 2016; Schirmer and Kotz, 2006). The current study probed valence-related interactions between emotion and attention during voice processing in schizophrenia, reflected in the P3b. Further, it examined the contributions of semantic information during top-down attention allocation to vocal emotional changes. We found that the emotional valence of vocal sounds modulated attention differently in schizophrenia patients compared to controls. Even though patients did not differ from controls in the processing of vocal threat (anger), they showed reduced P3b amplitude in response to happy vocal sounds, irrespective of whether speech semantic content was intelligible or not. Further, the processing of frequent (standard) neutral vocal sounds was similar in the patient and control groups, indicating that P3b abnormalities in the schizophrenia group were not explained by reduced inhibition of task-irrelevant information.

P300 amplitude modulations are thought to index the allocation of attention resources to a stimulus, thereby reflecting the relative salience of a stimulus to the individual (e.g., Pinheiro et al., 2017a). P300 amplitude reductions have been consistently reported in schizophrenia, indicating that these patients do not engage the same amount of processing resources as controls (Ford, 1999). Other studies revealed that P300 amplitude in schizophrenia might be increased by additional motivation. For example, the P3b to target letter stimuli was comparable to controls when standard and target letters were interspersed with task-irrelevant emotional pictures (Horan et al., 2012). Whereas prior studies reported reduced attention to happy stimuli (e.g., happy faces – Loughland et al., 2002; Schneider et al., 1995), others found increased processing of negative information in schizophrenia such as negative interpretation of ambiguous contextual information (Phillips et al., 2000), increased external misattribution errors for negative speech (Johns et al., 2001; Pinheiro et al., 2016), or stronger effects of negative relative to positive mood induction on cognitive processing (Pinheiro et al., 2015b). Alterations in the capacity to selectively direct attention to relevant stimuli in the environment based on their emotional salience may explain the P3b modulations observed in the current study.

The assignment of greater salience to vocal stimuli predicting an aversive (vs. appetitive) outcome may explain biased selective attention to angry compared to happy prosody in schizophrenia patients. According to the affect-biased attention hypothesis, top-down processes may bias attention toward specific acoustic cues based on what is motivationally relevant to the listener in a given context and/or previous experience (Pollak and Tolley-Schell, 2003; Todd et al., 2012). Along the same lines, the contextual or individual significance of a prosodic stimulus was found to modulate processing at all stages of emotional prosody processing (Schirmer and Kotz, 2006). We suggest that in the context of reduced P3b in response to different target types and tasks in schizophrenia, a negativity bias in voice perception in schizophrenia could explain the increased attentional resources allocated to the processing of vocal threat (anger) compared to vocal cues associated with affiliation (happiness), resulting in a similar P3b amplitude in response to angry prosody in patients and controls.

On the other hand, the reduced P3b to happy prosody in patients may reflect task-relevant decreased attention toward positive vocal information, i.e. a positive attenuation mechanism. Reduced allocation of attention resources to happy prosody may reflect reduced salience of positive vocal cues in schizophrenia patients. The finding reported here dovetails with the results of our earlier study where specific P2 abnormalities in response to happy prosodic words were found, indicating altered categorization of positively valenced emotional percepts as "salient" (Pinheiro et al., 2014). Further, it is consistent with impaired sustained attentional processing of pleasant (but not unpleasant) visual stimuli in schizophrenia (Horan et al., 2010). Decreased attention to positive information may contribute to decreased positive affect in patients with schizophrenia (Blanchard et al., 1998) and impact upon the processing of salient information when navigating social contexts (Hooker and Park, 2002; Niznikiewicz, 2013). Drawing on evidence that vocal emotional processing is modulated by attentional focus (Pinheiro et al., 2017b, 2017a, 2015a), later, attention-dependent processes (P300) may specifically contribute to impaired vocal emotional recognition.

It is worth noting that the semantic status of the word did not affect the interactions between emotion and attention, contrary to prior studies showing an influence of semantic information on early stages of emotional prosody processing (reflected in the N1 and P2 - Pinheiro et al., 2013, 2014). Hence, it is possible that semantic status affects earlier neuro-cognitive responses to prosodic speech but not higher-order evaluative processes that take place when decoding vocal emotions (Feingold et al., 2016).

P3b amplitude modulations were not significantly associated with clinical scores, illness duration or medication. This finding agrees with prior studies showing that emotional processing abnormalities occur irrespective of illness duration and are independent of antipsychotic medication (Edwards et al., 2001; Kucharska-Pietura et al., 2005). Even though prior studies evidenced a relationship between emotion recognition impairments and specific positive (e.g., hallucinations - Alba-Ferrara et al., 2012; Shea et al., 2007; Turetsky et al., 1998) or negative symptoms (Pfefferbaum et al., 1989; Preuss et al., 2010), this relationship has not been confirmed in other studies (e.g., Feingold et al., 2016; Jahshan et al., 2013; Vogel et al., 2016). It is plausible that behavioral measures, such as accuracy in emotion recognition, are more sensitive to the effects of specific clinical symptoms or medication (Ford, 2018). Nonetheless, the stage of the illness may have accounted for the current pattern of findings. For example, patients in remission showed decreased P3b in response to positive relative to negative stimuli visual stimuli when compared with patients in the acute phase (Yamamoto et al., 2001).

Some limitations of the current study should be noted, namely the relatively small sample size and the fact that only chronic medicated schizophrenia patients were tested. In addition, the small sample size could have accounted for the lack of significant associations between the P3b and clinical scores. Future studies should address these issues.

5. Conclusions

The current findings provide support for the hypothesis that higher-order operations reflected in P3b amplitude modulations are abnormal in schizophrenia in a valence-dependent manner: P3b was reduced in response to vocal changes with positive (happy) but not negative (angry) valence, irrespective of speech intelligibility. This finding indicates that top-down attentional resources were less strongly engaged by happy relative to angry speech prosody, reflecting alterations in the evaluation of the emotional relevance of the voice. Altered detection of vocal changes with a positive quality may lead to deficits in the comprehension of the emotional states and intentions of social partners during vocal communication.

These findings support the relevance of top-down attention-dependent training in social cognition remediation programs with a focus on emotion recognition (Potts et al., 1998).

Conflict of interest

All authors declare that they have no conflicts of interest.

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CRediT authorship contribution statement

Ana P. Pinheiro: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Visualization, Writing - original draft, Writing - review & editing. **Margaret Niznikiewicz:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing.

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