The deficit of multimodal perception of congruent and non-congruent fearful expressions in patients with schizophrenia: the ERP study.

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Abstract

Emotional dysfunction, including flat affect and emotional perception deficits, is a specific symptom of schizophrenia disorder. We used a modified multimodal odd-ball paradigm with fearful facial expressions accompanied by congruent and non-congruent sounds to investigate the impairment of emotional perception and reaction to other people's emotions. We analyzed subjective assessments and ERP data for emotionally charging congruent and non-congruent stimuli in patients with schizophrenia and healthy peers. The results showed the deficit of multimodal perception of fearful stimuli in patients with schizophrenia compared to healthy controls. The amplitude of N50 was significantly higher in subjects of the control group for non-congruent stimuli than congruent and did not differ in patients with schizophrenia. The dynamics of P100 and N200 components confirmed the impaired sensory gating in patients with schizophrenia. The lower amplitude of P3a could be associated with deficits in verbal memory and attention, less emotional arousal, or incorrect interpretation of emotional valence as specific features of patients. The difficulties in identifying the incoherence of facial and audial components of emotional expression could be significant in understanding the psychopathology of schizophrenia.

Keywords: EEG, event-related potentials, schizophrenia, fearful expressions, perception, non-congruent sounds

Introduction

Fear is one of six basic emotions that have considerable biological value. The emotional expressions of fear could be perceived and identified significantly easier than other emotions and the least affected in variable clinical populations. In particular, patients with variable mental or neurological diseases could correctly emit fear and anger prosody of speech and fearful facial expression however showed impairment in discrimination of happy expressions (Bonfils KA, 2019; Johnstone, 2006, Schneider. 1995; Kang, 2009). The reason for the privileged position of fearful stimuli during perception consisted of fear that generates danger signals and leads to the mobilization of the body's resources. In particular, the perception of fearful facial expressions usually was accompanied by heightened arousal, negative, or aversive subjective experience. It could enhance the visual processing of stimuli activating the sympathetic nervous system (Susskind et al., 2008; Kelley & Schmeichel, 2014). The other neural basis for visual perception enhancement could include the increased work of the amygdala triggering the brain areas involved in processes of directed attention and the visual cortex (Phelps, 2006)

Simultaneously, perception of fearful facial expressions in real life necessarily required multi-modal analysis, including facial expression and auditory accompaniment, such as screaming, moaning, or signing. Difficulties of multi-modal perception of fearful stimulation could be associated with the ambiguous interpretation of the perceived facial expression and emotional vocalizations typical for patients with schizophrenia. According to the previous studies, the perception of facial expressions plays an essential role in the clinical manifestations of schizophrenia, and perception and expression of emotions is an important marker for assessing the severity of the emotional impairment in patients with schizophrenia (McCleery, 2015; Andreasen 1984; Kay, Fiszbein et al. 1987). In particular, deficits of emotional perception in patients with schizophrenia had previously reported in a considerable body of literature that demonstrated a decrease in the accuracy of recognition of emotions modulated by voice by this group of patients (Globerson E., 2015), deficit of facial expression perception (Kring, Moran, 2008), as well as understanding and awareness of other emotional expressions required for successful social interaction (Berenbaum, Oltmanns, 1992; Deutsch, 1942). The ERP studies also demonstrated that impairment of emotion perception in patients with schizophrenia (Pinheiro, 2013). For example, the significantly higher error rate in identifying non-linguistic emotional sounds in patients suffering from schizophrenia was also reported (Tüscher, 2005) as well as deficits in visual processing for all types of emotional stimuli including fearful (Shah, 2018). However, the most pronounced dysfunction of emotional stimuli was detected during the presentation of multimodal stimuli such as facial expressions with emotions of joy, calm and fear simultaneously with congruent or non-congruent sounds (Müller, 2014). Other studies also suggested that deficits in facial information encoding extend to multimodal face-voice stimuli and that delays exist in feature extraction from multimodal face-voice stimuli in schizophrenia (Liu, 2016). so impairments in neural synchrony could be related to sensory demands and the processing of multimodal information (Moran, 2012) and were accompanied by ambiguous or incorrect interpretation of the perceived facial expression and emotional vocalizations. In our study we aimed to assess the ability of patients with schizophrenia to match the compliance of emotional stimuli presented simultaneously in visual and auditory modality using congruent and non-congruent to fearful expressions emotional sounds.

Methods

Participants sit in front of the screen. The instruction was to listen to a sound and watch on the screen. Two types of multimodal visual-voice stimuli with semantical incoherence were presented: the same emotion expression and incoherent emotion expression. There oddball passive paradigm was used while EEG event-related potentials (80% coherent and 20% incoherent). We made three trials of 2 conditions (coherent/incoherent) with three parameters

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(3 kinds of sound and image for the condition – to avoid addictive effect). Stimuli were presented in program PsychoPy v3.0.

Participants

Healthy volunteers were recruited through online or Institution advertisements. In total, 20 participants of the control group (mean = 26.3, SD = 5.32, 12 female, eight male) with no history of schizophrenia or schizoaffective disorder, intelligence quotient (IQ) less than 80, or medical illness associated with increased rates of depression completed the study. Participants gave written informed consent and received monetary compensation for their participation (500 Rubles).

Twenty-two patients with schizophrenia (mean = 28.1, SD = 5.19, 10 female, 12 male) were recruited via Alekseev's Psychiatric Clinical Hospital after a Diagnostic clinical interview (ICD-10) to determine the diagnosis. Inclusion criteria included individuals with a history of first or second psychosis. The severity of symptoms was assessed in participants using the Positive and Negative Syndrome Scale (PANSS) (average meaning 93.52±15.7).

All subjects were right-handed, had normal hearing level in both ears, and their intellectual skills were within the normal range. They had no history of neuropsychiatric disorders or head injury.

Ethical statement

The ethics board of the Institute of Higher Nervous Activity and Neurophysiology of RAS (IHNA) approved the study protocol. EEG recordings and stimuli assessment were conducted with the permission of the ethical board of Alekseev' Psychiatric Clinical Hospital. All participants provided written informed consent. The study followed the tenets of the Declaration of Helsinki.

Stimuli description

The visual stimuli consisted of centered monochrome images of scared women 800 x800 pixel jpeg images (see Figure 1 for examples). The images of scared women were purchased from the internet database (Can Stock Photo, Fotosearch) and International Affective Picture System (IAPS), then centered and normalized for color, brightness, contrast, background, and face size using Photoshop software.

The stimuli consisted of infant crying and laughter vocalizations which were purchased from the internet sound database (Sound Jay, Sound Library, Freesound, Soundboard). The raw audio files were downsampled at a rate of 44100 Hz to mono.wav files with 32-bit resolution. The sounds were presented using Presentation. All files were then normalized for root-meansquare (RMS) amplitude and were modified with respect to the stimulus length using Wavelab 10.0 (Steinberg).

24 original audio files (10 screaming vocalizations and 7 laughing) were submitted to pilot perceptual validation by nineteen adults (students) in the pilot experiment (average age = 20.1 years; SD = 3. 7; range = 19 – 25; 10 females; none of these participants took part in the main study). They were asked to rate each of the 14 stimuli presented in random order using following scales (0-10): "unpleasant-pleasant" and "arousal" and "hardly recognized – well recognized", "fearful". After pilot study we withdraw hardly recognized stimuli and selected sounds with highest rates of "pleasantness" (for laughter) and "fearful"(for screaming) with

most similar rates of "arousal" and most similar physical characteristics (duration, pitch and loudness)

Auditory stimuli were 1500 ms (±17 ms) in duration sounds of woman screaming and laughter equalized by the average pitch and loudness .

The standard (congruent) stimulus was the simultaneously presented image and sound of a screaming woman 1500 ms long. The deviant (non-congruent) stimulus simultaneously presented an image of a screaming (frightened) woman and the sound of her laughter 1500 ms long. We used three types of stimuli to exclude the addictive effect.

Procedure

Visual stimuli were presented for 1500 ms centrally on a 17" LCD monitor with 60 /120 Hz screen refresh rate, participants sat 80 cm away from the screen. The interstimulus interval randomly varied from 1000 ms - 2500 ms.

The task consisted of one standard (presented approximately 80% of the time or 120 times) and one deviant (presented approximately 20% of the time or 30 times) stimulus. The standard and deviant stimuli were presented in random order. Participants were instructed to "view and listen to stimulation, don't close eyes and try not to think about something special"

Figure 1. Visualization of used multimodal odd-ball paradigm Fig. 1. Experimental design.

Subjective assessment of stimuli

After the subject listened to the whole set, he was presented with the image of a sad face and the sound of crying (congruent stimulus) on the same monitor with the scales. On the scales of "sadness", "happy", "anger", "fear" and "calmness" from 1 to 9 it was required to evaluate the stimulus. After filling in the scales, four incongruent stimuli were presented, which the subject evaluated on the same scales. If difficulties arose in understanding the task, the subject was assisted by the researcher.

EEG registration

EEG was acquired using a 19-channel EEG amplifier Encephalan with the recording of polygraphic channels (Poly4, Medicom MTD, Taganrog, Russian Federation). The sampling rate was 250 Hz. The amplifier bandpass filter was nominally set to 0.05–70 Hz. AgCl electrodes (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, and O2) were placed according to the International 10–20 system. The electrodes placed on the left and right mastoids served as joint references under unipolar montage. The vertical EOG was recorded with AgCl cup electrodes placed 1 cm above and below the left eye, and the horizontal EOG was acquired by electrodes placed 1 cm lateral from the outer canthi of both eyes. The electrode impedances were kept below 10 kΩ. The EEG fragments did not contain any epileptiform activity (exclusion criteria).

Data analysis

The EEG data were processed using a 1.6–30 Hz bandpass filter (finite impulse response filter). The 50 Hz power frequency noise was subject to notch processing. The reference electrode was changed to a global brain average reference. Artifacts due to eye movement were excluded by independent component analysis. Further data analysis included several stages.

First, segments of interest were located within the whole data file and extracted with encephalograph proprietary software Encephalan EEGR 19/26.

For the ERP analyses, the EEG data were analyzed and processed using EEGLAB 14.1.1b, which is a neural electrophysiological analysis tool based on MATLAB (MathWorks, Natick, MA, United States). The EEG was segmented from 100 ms prior to initiation to 800 ms after the stimulus onset. Amplitude and latency of each component were calculated for each participant in both groups separately for statistical analysis.

Event-related potential (ERP) analysis

Amplitude and latency of each component were calculated for each participant in both groups separately for statistical analysis. For the ERP analyses, the EEG data were analyzed and processed using EEGLAB 14.1.1b, which is a neural electrophysiological analysis tool based on MATLAB (MathWorks, Natick, MA, United States). The EEG data were processed using a 1.6–30 Hz bandpass filter (finite impulse response filter). The 50 Hz power frequency noise was subject to notch processing. The reference electrode was changed to a global brain average reference. Artifacts due to eye movement were excluded by independent component analysis. The EEG was segmented from 100 ms prior to initiation to 800 ms after the stimulus onset. In this study, the amplitudes and latencies of N50, P100, N200, P3a, P3b were measured and analyzed. Based on the topographical distribution of the grand-averaged ERP activity the following sets of electrodes for each component were chosen: Fz, F3, F4, Cz, C3, C4 were selected for the analysis of N50 (30–90 ms) and P100 component (90–160 ms); N200 (160-250 ms), at the Fz, F3, F4, Cz, C3, C4, Pz, P3, P4, O1, O2 electrode sites, P3a (220-300 ms) were analyzed at the F3, Fz, F4, Cz, C3, C4 electrode sites and P3b components (250–500 ms) at the Cz, C3, C4, Pz, P3, P4, O1, O2.

Statistical analysis

Statistical analysis was carried out with STATISTICA 13. Differences between groups, differences in amplitudes, and latencies of ERP components, as well as subjective ratings, were assessed using a nonparametric Mann-Whitney u-test followed by post-hoc comparison (Bonferroni, $p < 0.05$). The repeated-measures ANOVA was used to assess separately for the attraction of two effects: condition (standard stimulus and deviant stimulus)* group.

The correlation analysis between subjective ratings and ERP data was calculated using Spearman rank correlations with Bonferroni correction ($p < 0.05$) separately for each group of subjects. The inside group differences between amplitude and latency of ERP components of congruent and non-congruent stimuli for each ERP component were calculated using non-parametrical Wilcoxon rank tests.

Results

Differences in subjective ratings of stimuli

Groups didn't differ in their individual rates of self-assessments by scales "Sad", "Happy", "Angry", "Scared" and "Relaxed". Non-congruent stimuli were assessed as being happier by patients, than subjects of control group (z=2.6, p=0.008), controls had 2.2 ± 1.8 scores by scale "happy" assessing non-congruent stimuli versus 5.3 ± 2.1 scores in patients.

Group differences in ERP data

Patients had longer latency of N50 for both congruent (Mann-Whitney U Test; z=2.8, p = 0.004) and non-congruent stimuli (z=2.6, p = 0.008), lower amplitude of N50 for non-congruent stimuli (z=-2.9, p = 0.001), larger amplitude of P100 for non-congruent stimuli (z=2.1, p = 0.03), larger amplitude of N200 (z=2.4, p = 0.02), lower amplitude of P3a for both congruent (z=-2.2, p = 0.03) and non-congruent stimuli (z=-2.3, p = 0.02), lower amplitude of P3b for non-congruent stimuli (z=-2.4, p = 0.01)   (see Figure*, Table*)

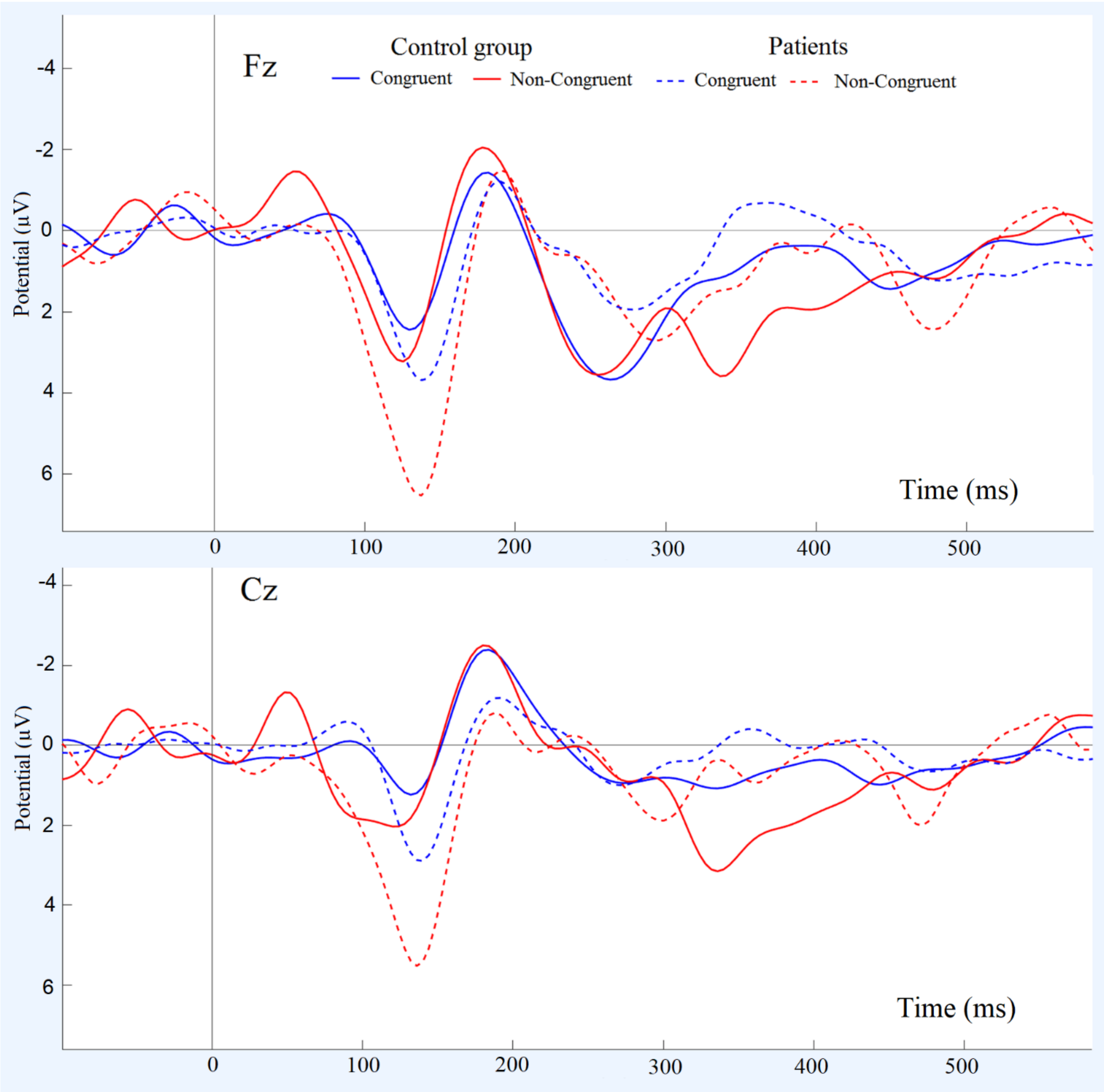

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Figure 2. ERPs for congruent and non-congruent stimuli in two electrode sites (Fz, Cz) for two groups (patients with schizophrenia and healthy controls) Potential (µV)

Differences between congruent and non-congruent stimuli

The amplitude of N50 was significantly higher in the control group subjects for non-congruent stimuli than congruent; patients did not show the difference of N50 amplitude between congruent and non-congruent stimuli (Repeated measures ANOVA stimuli*group $F(1, 40)=6,3628$, $p=,008090$). Both groups of subjected demonstrated longer latency of P100 for congruent stimuli compared to non-congruent (stimuli effect; $F(1, 40)=8,8266$, $p=,00729$). Both groups of subjected demonstrated lower amplitude of P3b for congruent stimuli compared to non-congruent (stimuli effect; $F(1,40)=15,857$, $p=,00068$).

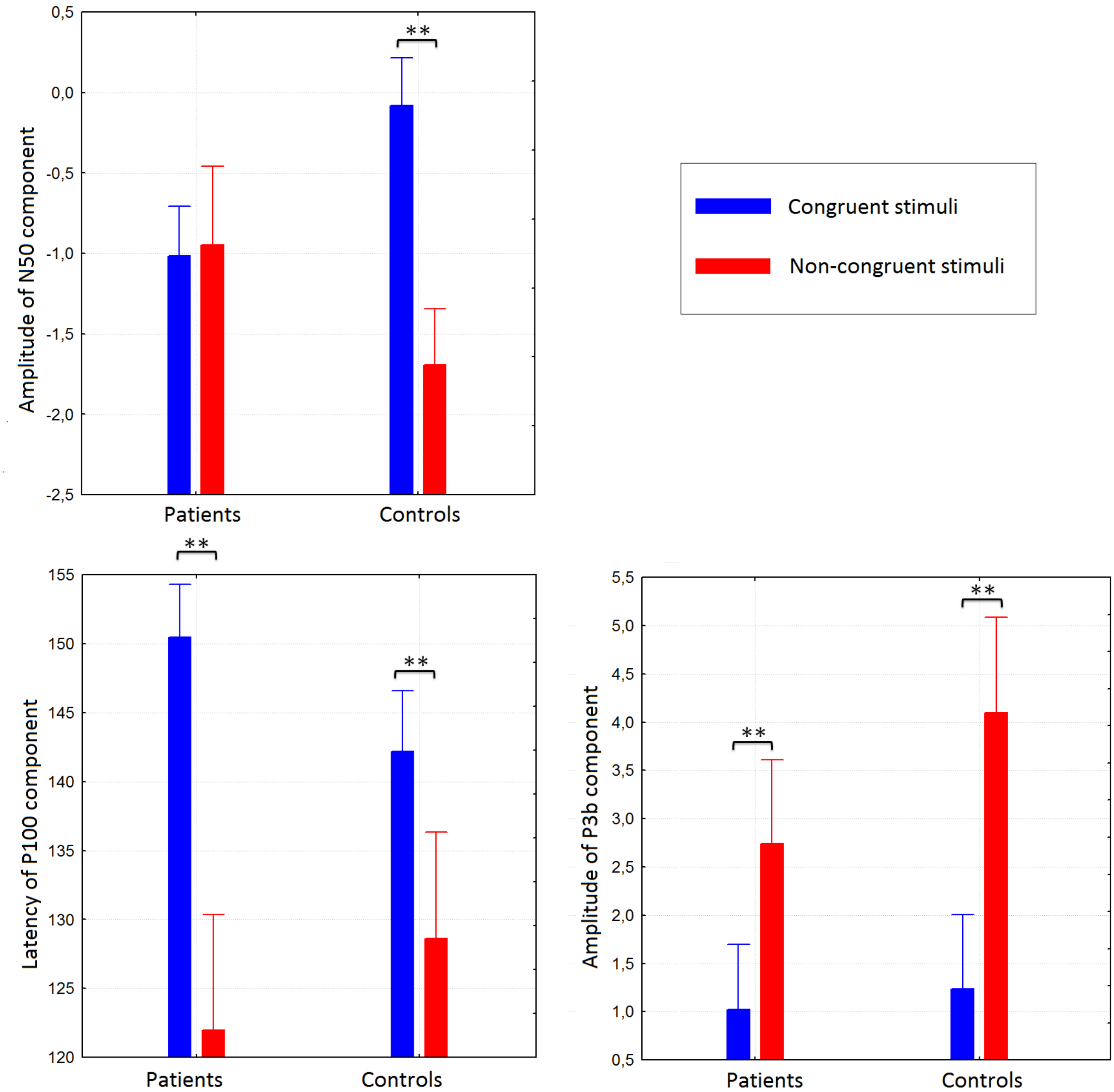

*Figure 3. Values of amplitudes and latencies of N50, P100 and p3b ERP components for two groups (patients with schizophrenia and healthy controls) averaged as described in section "Event-related potential (ERP) analysis". The significant differences (p<0.01) were marked by "**"*

Correlations between ERP and subjective ratings and PANSS

The amplitude of P100 for both congruent (r=0.65, p = 0.01) and non-congruent stimuli (z=0.59, p = 0.03) correlated with PANSS scores. Scores of self "calm" in group of patients negatively correlated with latency of P100 (r=-0.73, p = 0.008), N200 (r=-0.83, p = 0.005) and P3a (r=-0.83, p = 0.006) components for congruent stimuli. The amplitude of P3b for non-congruent stimuli negatively correlated with happiness of stimuli in group of patients (r=-0.81, p = 0.007) and didn't reach significance in healthy controls (z=-0.52, p = 0.06).

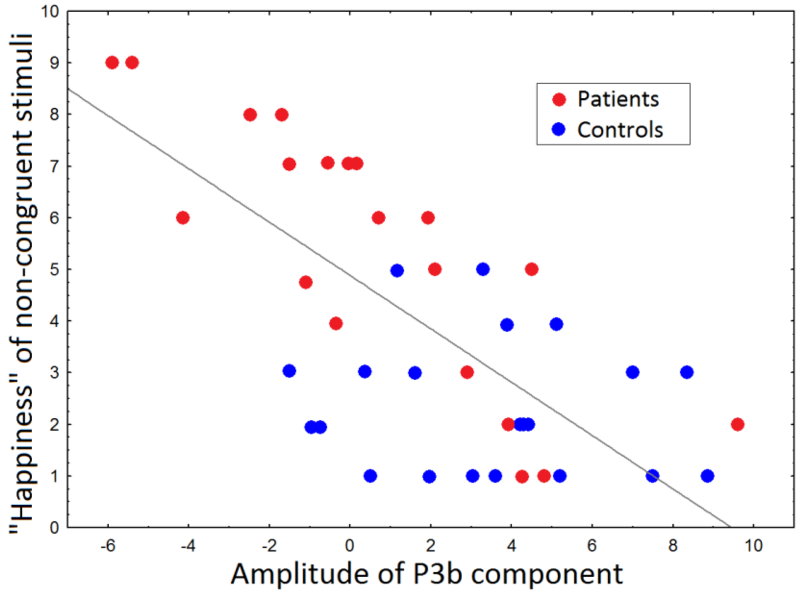

Figure 4. Scatter-plot of individual values demonstrated significant correlation between the amplitude of P3b happiness of non-congruent stimuli in group of patients.

Discussion

We identified that the amplitude of N50 was significantly higher for non-congruent stimuli only in subjects. In contrast, patients had reduced N50 amplitude and longer latency both for congruent and non-congruent stimuli. As was shown previously, the early negative component around 50 ms (N50) was generated in the auditory cortex as a response for the rare stimuli and was associated with the encoding of the multimodal information (Fellinger, 2012). Other studies reported that the appearance of N50 could be modulated by percept repetition (de Jong, 2014) and was associated with the perception of angry, happy, or sad facial expressions (Tsalamlal, 2018). So, the difference between congruent and non-congruent stimuli, which was found in healthy controls and reduced in patients with schizophrenia, could be explained by, first, early sensory abnormalities during emotional recognition (Tsalamlal, 2018), and second, by the deficit of implicit perceptual memory which modulated early processing of multimodal stimuli (de Jong, 2014; Jackson, 2001).

The larger amplitude of P100 and N200 components correlated with PANSS scores, which was found in a group of patients, could be explained by the well-known sensory gating effect usually reduced in patients with schizophrenia (Budnick & Braff, 1992). Previous studies showed that the amplitude of early components of multimodal ERPs should be typically decreased compared to ERP for single modality (Giard & Peronnet, 1999). The origin for the decrease of ERP components' amplitude could be explained by the sensory gating phenomenon revealed in multisensory studies (Lebib, 2003). We hypothesized that the sensory gating effect was the reason for the lower amplitude of the components N200, P100 in subjects of the control group, and the lack of sensory gating provided the absence of amplitude' decrease in patients with schizophrenia (Boutros, 2005). The previous findings could explain the origin of these group differences between patients and the control group, demonstrated that multisensory integration requires the connections between unisensory and polysensory brain regions, which could be impaired in patients with schizophrenia (Aine, 2017). The difference of assessment of congruent and non-congruent stimuli that was significantly higher in control group subjects and more stable in the group of patients correlated with a difference of P100's amplitude for congruent and non-congruent stimuli in the left temporal area. The P100's amplitude was shown to reflect general primary visual analyses in the striate and cortex (Gomez Gonzalez, 1994). It was also sensitive to the perception of emotionally charging visual stimuli (Eimer & Holmes, 2007). In our study, only healthy subjects showed a significant increase of the amplitude of P100 to deviant stimuli compared to standard. The lower amplitudes of P100 with no differences between congruent and non-congruent stimuli in patients with schizophrenia were consistent with previous findings, which demonstrated a decrease of the amplitude of P100 in patients with schizophrenia during the processing of emotional faces compared to healthy peers (Campanella, 2006). The reductions in P100 amplitude to emotional compared to neutral faces were revealed in patients with low-to-medium shyness (Jetha, 2013) and children with ASD (Stroganova, 2013). The absence of the P100's changes in patients with schizophrenia could be explained by the impaired processing of emotional stimuli that were not modulated by the emotional identity of faces compared to healthy controls (Thoma, 2014).

The deficit of implicit perceptual memory and attention in a group of patients was also revealed for the late ERP components. In particular, we found that patients had a lower amplitude of p3a for both congruent and non-congruent stimuli. According to the previous findings, the reduction of P3a could be described as reliable biomarkers of schizophrenia and was associated with deficits in verbal memory and attentional switching, reflecting dysfunctions in the temporal and frontal systems (Hermens, 2010). At the same time, the reduction of P3a in patients with schizophrenia could be associated with less emotional arousal during emotional perception or incorrect interpretation of emotional valence. In particular, this ERP component was reported to be reduced in the early stages of a psychotic illness experienced by disturbances in perception and affect (Atkinson, 2012; Schultze-Lutter, 2012). Whereas in healthy controls, the enhanced P3a amplitudes in response to unpleasant pictures were revealed, and its amplitude was sensitive to the arousal value of the stimulation (Delplanque, 2006).

The perception of non-congruent stimuli was accompanied by a higher rate of their "happiness" in a group of patients. In particular, the scared face expressiveness with laughter's sound accompaniment was assessed as being happier by patients than healthy controls. Moreover, these subjective rates were negatively associated with the amplitude of P3b, which was higher P3b for non-congruent stimuli in both groups of subjects but achieved significance only in patients with schizophrenia. According to the previous findings, the amplitude of P3b could be related to expression categorization (Calvo & Beltrán, 2014; Campanella, 2010); moreover, the P3b component was shown to be modulated by the emotional arousal and the valence of the non-congruent pictures (Delplanque, 2005). At the same time, in our study, the picture demonstrated fearful expression. As we revealed, the analysis of stimuli and assessing its happiness in healthy controls was based predominantly on visual stimulus, unlike a group of patients. Our results demonstrated that audio-visual cross-modal processing in patients with schizophrenia was predominantly modulated by the affective arousal and valence of non-congruent sound and less picture.

Conclusions

Summarizing our results, we found that patients with schizophrenia demonstrated a deficit of multi-modal perception of fearful stimuli than healthy controls. These difficulties were revealed both for the early and late stages of stimuli processing. Comparing to healthy controls, patients had reduced amplitude of N50 for non-congruent stimuli associated with sensory abnormalities and the deficit of implicit perceptual memory during emotional multi-modal recognition. Patients with schizophrenia also had higher amplitude of P100 and N200 components that could be explained by impaired sensory gating and reduced lower amplitude of P3a could be associated with deficits in verbal memory and attention, less emotional arousal, or incorrect interpretation of emotional valence. Finally, our findings demonstrated the impairment of audio-visual multi-modal perception in patients with schizophrenia during the processing of non-congruent stimuli was associated with their focus on the arousal and valence of sound, correlated with the amplitude of P3b. Whereas subjects of the control group during the processing of multi-modal stimuli perceived, first, fearful facial expressions and, second, the non-congruent sound

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

Author Contributions

Those who conceived and designed the study include GVP, AVM, NVZ and OVM. AVM, GVP and NVZ performed the experiments. AVM and GVP analyzed the data. GVP and AVM wrote the article.

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