Electrophysiological examination of visual perception and emotion recognition in schizophrenia

Doctoral theses

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1. INTRODUCTION

Schizophrenia is an intensively studied, complex, heterogeneous mental disease characterized by a diverse psychopathology. Treatment is aimed not only to improving psychotic symptoms, but also a wide range of clinical, psychological and social aspects that contribute to the achievement of independent and autonomous living.

Social cognition involves the perception, processing and use of social information to understand the intentions of others and to guide our social interactions. Impaired social cognition in schizophrenia makes difficult to identify emotions, form social relationships and it is related with the patients' the quality of life.

In this thesis, we analyzed the electrophysiological correlates of early visual perception, face and object recognition (house) and emotion recognition. A large amount of data is available on the evoked potentials associated with these processes; however, these studies provide limited information on neural activity, whereas event-evoked spatial perturbation analyses provide insight not only into evoked but also into induced neural activity. Electrophysiological activity within the theta range (4-7 Hz) plays a crucial role in emotion identification, therefore the theta frequency band was investigated in the data analysis.

According to the bottom-up model the early sensory deficits lead to higher level process -facial affect recognition- impairments, which further contribute to the psychosocial functioning deficits in schizophrenia. The three paradigms examine different levels of visual perception, separately, but these paradigms build on each other provide the opportunity to further investigation of the bottom-up theory. A better understanding of bottom-up model may contribute to a more precise understanding of the neural mechanisms underlying neuropsychiatric and behavioral disorders.

2. OBJECTIVES

In this thesis, we have analyzed the different levels of visual perception in schizophrenic patients and healthy controls using three paradigms.

We sought to answer these questions within each paradigm:

1. Is there a difference in theta synchronization during the presentation of simple, elementary visual stimuli between schizophrenic patients and control group?
2. Is there a difference in theta synchronization during the presentation of faces and houses between schizophrenic patients and control group?
3. Is there a difference in theta synchronization when presenting faces expressing emotion between schizophrenic patients and control group?
4. Is there any connection between the supposed difference (in theta synchronization) and the behavioral results of emotion recognition and symptom severity of schizophrenia?

We had two competing hypotheses:

1. According to our first hypothesis we expected that theta synchronization in the magnocellular biased condition correlated with theta synchronization in face and

emotion recognition conditions. This hypothesis is consistent with the bottom-up model of schizophrenia.

2. According to our second hypothesis no such correlation would be found, which may raise the possibility that these two impairments occur independently in schizophrenia, i.e. they are separate biomarkers of the disorder.

3. METHODS

Altogether 39 patients with schizophrenia and 40 healthy controls matched in age, gender and education participated in the study. EEG was recorded using a 128-channel Biosemi ActiveTwo high electrode density amplifier system with a sampling rate of 1024 Hz. During the EEG recording, the subjects were instructed to sit in a comfortable chair in front of a table with a computer screen at a distance of about 50 cm, we used Presentation 13.0 software for stimuli presentation. For offline data analysis, we used built-in and proprietary Matlab functions and the free-to-use toolkit of the EEGLAB software.

3.1. Tasks

3.1.1. The visual task

In the visual-paradigm, low- (LSF) and high spatial frequency (HSF) Gaussian patches - Gaussian curve-weighted planar representations of spatial sine waves - were presented while participants focused on faces with neutral emotional charge presented in a randomized order. A total of 112 high- and 112 low-spatial-frequency Gabor patches were presented.

3.1.2. The face, non-face task

In the face-non-face paradigm, photographs of faces and houses were presented in randomized order. The task required participants to indicate whether they saw a face or a house by pressing a button. In the task, 80 faces and 80 houses were presented.

3.1.3. The emotion recognition task

In the emotion recognition paradigm, 80 happy, 80 sad and 80 emotionally neutral faces were selected from the Karolinska Directed Emotional Faces (KDEF) image collection. Subjects were instructed to press a button indicating whether the face is happy, sad or neutral.

3.2. Data analysis

The channels were divided into 5 regions of interest (ROIs): a frontal, a central, a mid-occipital, and two parieto-occipital regions.

Stimulus-related theta (4-7 Hz) activity changes were measured by event-related spectral perturbation (ERSP).

The different effects on ERSP were tested by three-way analyses of variance (ANOVA) of study group (healthy control (HC) vs. schizophrenia (SZ)) × ROI (a frontal, a central, a mid-occipital, and two parieto-occipital) × stimulus type (HSF vs. LSF or face vs. non-face or sad vs. neutral vs. happy). All the main effects and the 2-way and 3-way interactions are included into the ANOVA model. Since between-group comparisons were evaluated over five regions, Hochberg correction for multiple comparisons was applied to the post-hoc contrasts.

The associations of emotion recognition performance with ERSPs were investigated by Spearman correlation, since emotion recognition measures deviated from the normal distribution. For the same reason correlations of CPZ equivalent doses and PANSS scores with ERSPs were also investigated by Spearman correlation.

4. RESULTS

4.1. Visual task

There was a significant main effect of study group ($F(1,77) = 10.87$, $p = 0.0015$) on theta ERS, indicating a decreased theta synchronization in patients relative to controls. Region also had a significant effect on theta ERS ($F(4,77) = 20.15$, $p < 0.0001$). A significant main effect of stimulus condition ($F(1,77) = 11.45$, $p < 0.001$) was also detected indicating a stronger theta ERS to LSF ($t = 3.62$, $df = 77$, $p = 0.0005$, in right-parieto-occipital region) compared to HSF condition.

The 2-way interaction of study group and stimulus condition was also significant ($F(1,77) = 9.65$, $p = 0.003$). This interaction was analysed further by post hoc t comparisons indicating that theta ERS for LSF stimulus condition was decreased in patients relative to controls ($t = 3.59$, $p = 0.0006$), while no similar between group difference was found for the HSF stimulus condition ($t = 1.54$, $p = 0.13$).

4.2. Face, non-face task

There was a significant main effect of study group ($F(1,76) = 6.88$, $p = 0.011$) on theta ERS in the 140–240 ms time window, indicating decreased synchronization in the theta range in patients relative to controls. Region also had a significant effect on theta ERS ($F(4,76) = 23.63$, $p < 0.0001$). A significant main effect of stimulus condition ($F(1,76) = 20.19$, $p < 0.0001$) was also detected indicating a stronger theta ERS to face compared to house conditions. None of the interactions had a significant effect ($p>0.1$).

Effect size in term of cohen's d (cohen's d = mean1 - mean2/ ((SD1 + SD2)/2); /1 = face, 2 = non-face/) in the right-parieto-occipital region between conditions (face vs. house) in the control group was 0.41 and in the schizophrenia group 0.29, separately.

After covarying for the LSF - HSF difference in the analysis of the face non-face task the group difference did not remain significant ($F(1,75) = 2.71$, $p = 0.1$), while the LSF-HSF difference ($F(1,75) = 44.15$, $p < 0.0001$) had a significant effect on theta ERS.

4.3. Emotion recognition task

In the emotion recognition task, the difference between hit rates of controls (mean hit rate = 89.1% SD = 3.7) and patients with schizophrenia (mean hit rate = 80.3%, SD = 10.7) was significant ($U = 324$, $p < 0.001$). Reaction time in patients was significantly longer ($t=2.97$, $p=0.004$).

There was a significant main effect of study group ($F(1,75) = 8.5$, $p = 0.0047$) on theta ERS in the 140–200ms time window, indicating stronger synchronization in the theta range in controls relative to patients.

After covarying for the LSF - HSF difference in the analysis of the emotion recognition task the group difference did not remain significant ($F(1,74) = 2.99$, $p = 0.09$),while the LSF-HSF difference ($F(1,74) = 53.63$, $p < 0.0001$) had a significant effect on theta ERS.

4.4. Correlation

Theta activity in LSF condition (magnocellular biased) correlated significantly with theta activity in face non-face task in control group (face: $r = 0.57$, $p = 0.0001$; house: $r = 0.59$, $p < 0.0001$) and in schizophrenia group (face: $r = 0.42$, $p = 0.009$; house: $r = 0.57$, $p = 0.0002$). In contrast the correlations between theta activity in HSF condition (parvocellular biased) and in face condition were not significant in any study groups ($p > 0.05$).

Theta activity in the LSF condition (magnocellular biased stimuli) correlated significantly with theta activity in the emotion recognition task in the control group (sad: $r = 0.67$, $p < 0.0001$; neutral: $r = 0.61$, $p < 0.0001$; happy: $r = 0.67$, $p < 0.0001$) and also in the schizophrenia group (sad: $r = 0.62$, $p < 0.0001$; neutral: $r = 0.58$, $p = 0.0002$; happy: $r = 0.56$, $p = 0.0003$). In contrast correlations between theta activity in HSF condition (parvocellular biased stimuli) and in emotion recognition were not significant in any of the study groups ($p > 0.05$).

Theta ERS in the face condition correlated significantly with theta activity in the emotion recognition task in the control group (sad: $r = 0.83$, $p < 0.0001$; neutral: $r = 0.84$, $p < 0.0001$; happy: $r = 0.83$, $p < 0.0001$) and also in the schizophrenia group (sad: $r = 0.83$, $p < 0.0001$; neutral: $r = 0.75$, $p < 0.0001$; happy: $r = 0.83$, $p < 0.0001$).

Theta ERS in the house condition correlated significantly with theta activity in the emotion recognition task in the control group (sad: $r = 0.72$, $p < 0.0001$; neutral: $r = 0.71$, $p < 0.0001$; happy: $r = 0.70$, $p < 0.0001$) and also in the schizophrenia group (sad: $r = 0.71$, $p < 0.0001$; neutral: $r = 0.63$, $p < 0.0001$; happy: $r = 0.65$, $p < 0.0001$).

In the patient group emotion recognition task performance correlated significantly with theta ERS to (magnocellular biased) LSF condition (total hit score: $r = 0.35$, $p = 0.03$), but not correlated with ERS to (parvocellular biased) HSF condition (total hit score: $r = 0.12$, $p = 0.45$).

Also in the patient group significant correlations were found between emotion recognition task performance and theta ERS in the emotion recognition paradigm in the sad condition (total hit score: $r = 0.36$, $p = 0.03$), in the neutral condition (total hit score: $r = 0.37$, $p = 0.02$) and also in the happy condition (total hit scores: $r = 0.33$, $p = 0.049$). Moreover, theta ERS in face condition (in the face/house task) correlated significantly with the behavioral results (total hit score: $r = 0.36$, $p = 0.03$).

In the control group the correlation between emotion recognition task performance and theta ERS in any tasks did not reach the significance ($p > 0.05$).

No correlation was found between theta ERSs and clinical variables such as PANSS scores, antipsychotic doses in term of CPZ equivalents ($p > 0.05$).

5. CONCLUSIONS

Human faces and especially facial expressions are extremely important for social communication and the communication of our emotional states. In my dissertation, we investigated the bottom-up model in three study paradigms using event-evoked spectral perturbation (ERSP) analysis.

In our first paradigm, early visual perception was investigated by presenting Gabor patches of different spatial frequencies, with low spatial frequency used to stimulate the magnocellular pathway system and high spatial frequency used to stimulate the parvocellular system. In the patient group we observed decreased theta ERS to low- spatial frequency stimuli, confirming the previously described deficit in the magnocellular pathway.

In the second paradigm, object recognition, and thus a - higher level of visual stimuli processing - was investigated by presenting faces and buildings to the subjects. Subjects with schizophrenia responded with decreased theta ERS to both facial and non-facial stimuli compared to the control group.

In the third paradigm, we investigated the emotion recognition by presenting happy, sad and neutral faces. In the emotion recognition task a decreased theta ERS was found to all emotion conditions in the patient group relative to controls.

Theta ERS in the magnocellular biased (LSF) condition showed significant correlation with theta ERS to face, to non-face, and also to emotional face stimuli in both study group, these results confirmed that early visual perceptual abnormalities are associated with impaired emotion recognition.

Our results support the growing evidence to the bottom-up model of disrupted cognition in schizophrenia which indicate that early sensory deficit contribute to the impaired higher level dysfunction.

6. PUBLICATIONS

6.1. PUBLICATIONS RELATED TO THE DISSERTATION

Marosi C, Fodor Z, Csukly G. (2019) From basic perception deficits to facial affect recognition impairments in schizophrenia. Scientific Reports, 9: 8958.

6.2. OTHER PUBLICATION

Siraly E, Szabo A, Szita B, Kovacs V, Fodor Z, **Marosi C**, Salacz P, Hidasi Z, Maros V, Hanak P, Csibri E, Csukly G. (2015) Monitoring the Early Signs of Cognitive Decline in Elderly by Computer Games: An MRI Study. Plos One, 10.

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Szabo AG, Farkas K, **Marosi C**, Kozak LR, Rudas G, Rethelyi J, Csukly G. (2017) Impaired mixed emotion processing in the right ventrolateral prefrontal cortex in schizophrenia: an fMRI study. Bmc Psychiatry, 17.

Fodor Z, **Marosi C**, Tombor L, Csukly G. (2020) Salient distractors open the door of perception: alpha desynchronization marks sensory gating in a working memory task. Scientific Reports, 10.