The Neurophysiological Features of Anticipation in Schizophrenia: A Cross-Sectional Study of Event-Related Potentials

Нейрофизиологические особенности антиципации при шизофрении: исследование потенциалов мозга, связанных с событиями

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Original research

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ABSTRACT

BACKGROUND: It is known that disorders of mental activity in schizophrenia patients may be caused by an impairment in the actualization of past experience during anticipation (prediction), which leads to impairment in constructing predictions, comparing incoming sensory information with the predictions, and updating the predictions. Previous studies have shown that the probability of an expected event affects the components of event-related potentials in mentally healthy individuals. However, it has not yet been studied how changes in the probability of an expected stimulus influence the behavior of individuals with schizophrenia and their event-related potential measures.

AIM: To compare the influence of event probability on the characteristics of brain potentials in patients with schizophrenia and healthy individuals.

METHODS: The study included mentally healthy individuals and male schizophrenia patients. Electroencephalograms were recorded while participants performed a saccadic task within the Central Cue Posner's Paradigm under conditions of varying probability (50% and 80%) of target stimulus presentation. Pre-stimulus (Contingent Negative Variation) and post-stimulus (Mismatch Negativity and P3) components of event-related potentials were analyzed upon the presentation of two types of target stimuli: standard (presented on the same side as the cue stimulus) and deviant (presented on the opposite side), under conditions of 50% and 80% stimulus congruence probability.

RESULTS: The study involved 20 mentally healthy individuals and 18 schizophrenia patients. In healthy subjects, the amplitude of the contingent negative variation increased with high stimulus congruence probability, while the amplitude of the Mismatch Negativity (MMN) and P3 component was higher for deviant stimuli under conditions of high (80%) probability. In schizophrenia patients, changes in probability demonstrated no impact on the amplitude of the contingent negative wave, MMN, or P3.

CONCLUSION: The characteristics of event-related potentials in patients with schizophrenia indicate impaired anticipation processes.

АННОТАЦИЯ

ВВЕДЕНИЕ: Известно, что расстройства психической деятельности у больных шизофренией могут быть обусловлены нарушениями актуализации прошлого опыта в процессе антиципации (прогнозирования), которые приводят к нарушениям построения прогноза, сопоставления поступающей сенсорной информации с прогнозом и коррекции прогноза. Ранее было показано, что у здоровых людей вероятность ожидаемого события влияет на компоненты вызванных потенциалов головного мозга. Однако до сих пор не изучено, как изменение вероятности ожидаемого стимула влияет на поведение и мозговые ответы у лиц с шизофренией.

ЦЕЛЬ: Сравнить влияние вероятности событий на характеристики мозговых потенциалов у пациентов с шизофренией и здоровых людей.

МЕТОДЫ: В исследование были включены психически здоровые лица и больные шизофренией мужского пола. При выполнении участниками саккадической задачи в парадигме пространственной сигнализации в условиях разновероятностного (50 и 80%) предъявления целевого стимула регистрировались электроэнцефалограммы. Проанализированы достимульные (условная негативная волна) и постстимульные (негативность рассогласования и P3) компоненты связанных с событиями потенциалов мозга при предъявлении двух типов целевых стимулов: стандартные (предъявляемые с той же стороны, что и сигнальный стимул) и девиантные (предъявляемые с противоположной стороны) в условиях 50 и 80% вероятности совпадения стимулов.

РЕЗУЛЬТАТЫ: В исследовании приняли участие 20 психически здоровых лиц и 18 больных шизофренией. У психически здоровых лиц амплитуда условной негативной волны увеличивалась при высокой вероятности совпадения стимулов, амплитуда негативности рассогласования и компонента P3 была выше при девиантных стимулах в условиях высокой (80%) вероятности. У пациентов с шизофренией изменение вероятности не оказывало влияния на амплитуду условной негативной волны, негативности рассогласования и P3.

ЗАКЛЮЧЕНИЕ: Характеристики связанных с событиями потенциалов мозга у больных шизофренией указывают на наличие у них нарушений процессов антиципации.

Keywords: *schizophrenia; anticipation; predictive coding; event-related potentials*

Ключевые слова: *шизофрения; антиципация; прогностическое кодирование; связанные с событиями потенциалы мозга*

INTRODUCTION

Theoretical and experimental studies have shown that psychiatric disorders in schizophrenia patients are, in part, underpinned by a disruption in the actualization of previous experience [1, 2]. Reliance on experience is one of the fundamental requirements for anticipation, which is the process of foreseeing or predicting events. Therefore, the study of anticipation processes is essential for understanding the mechanisms underlying psychopathological symptoms in schizophrenia patients. In recent years, the theory of predictive coding has frequently been used to explain the mechanisms of anticipation and the symptoms of schizophrenia [3, 4]. According to this theory, the brain is a hierarchically organized system that performs probabilistic (Bayesian) inferences about future events by comparing incoming sensory information with preceding predictions, with the aim of minimizing prediction errors — discrepancies between predictions and sensory data [5, 6]. In schizophrenia patients, abnormalities in the brain regions involved in predictive coding have been demonstrated to result in sensory, motor, and cognitive disorders, as well as to disorders in the systems responsible for salience attribution and reward expectation. The development of psychopathological symptoms in patients with schizophrenia may be attributable to these abnormalities [4, 7, 8].

The predictive coding theory has explained some neurophysiological phenomena, particularly event-related potentials (ERP). Thus, mismatch negativity (MMN) is considered one of the key indicators of prediction error generation. In the classical methodology [9], MMN

is recorded in the auditory modality during passive (unattended) listening to auditory stimuli in an oddball paradigm. It appears as a negative peak in the amplitude of the difference wave (obtained by subtracting the event-related potential to standard stimuli from the ERP to deviant stimuli) approximately 100–250 ms following stimulus presentation. The appearance of MMN indicates that a pattern in the stimulus sequence has been identified, and that deviations from this pattern have been detected. This phenomenon is widely regarded as a signal of prediction error [10]. Reduced MMN amplitude is one of the most consistent electrophysiological signs of schizophrenia [11] and a primary indicator of impaired predictive coding mechanisms [8, 12]. It is known that in individuals without mental illnesses, MMN in the passive oddball paradigm does not differ from that in the active variant, when the subject's attention is directed towards the stimuli [13–15]. This confirms the assumption that the MMN reflects pre-attentive processes involved in discriminating sensory stimuli and automatically detecting changes in their parameters [16, 17]. Thus, the MMN can be associated with a prediction error that is generated due to deviations in local regularities related to stimulus characteristics [18]. Visual MMN is more pronounced in the occipital and parietotemporal regions [19] and is also reduced in patients with schizophrenia [20].

In addition to the MMN, the P3 component of the ERP is recorded in the active oddball paradigm. This positive component occurs between 250 and 500 ms after the presentation of a deviant stimulus. The P3 amplitude in schizophrenia patients is lower than that in individuals without mental disorders [21]. MMN and P3 are considered to index different stages of discrepancies detection between predictions and sensory data [22]. Whereas MMN reflects the detection of local deviations tied to specific details of incoming information that fail to match predictions (e.g., pitch, brightness, motion trajectory), P3 reflects the processing of generalized information related to stimulus selection and/or evaluation, incorporating global deviations associated with complex patterns (e.g., differences between sequences comprising a specific number of stimuli) [18].

Anticipation (prediction) processes are also reflected by such a neurophysiological phenomenon known as the contingent negative variation (CNV). The CNV is characterized by a gradual buildup of negative potential in frontal-central brain regions occurring between two interrelated stimuli: a cue/warning stimulus (S1) and a trigger/target stimulus (S2) [23]. CNV is thought to represent preparatory processes related to the pre-tuning and optimization of the brain systems involved in a particular task [24, 25]. The amplitude of the CNV could reflect the processes of anticipation of stimulus S2, which are triggered by the presentation of stimulus S1 [26]. During the anticipation of the subsequent stimulus, the amplitude would increase if the target stimulus corresponded to the cue, and decrease if the target stimulus violated the established rules [27]. In patients with schizophrenia, the amplitude of CNV is lower in comparison to in individuals without mental disorders. Furthermore, a disruption of the CNV topography has also been observed in these patients [28–30]. Based on the predictive coding theory, a reduced CNV amplitude may be indicative of an insufficiency in expectations and predictions concerning upcoming events, as well as an impaired ability to utilize contextual information in making predictions [31].

Studies of predictive coding processes using the Central Cue Posner Paradigm (CCPP) have shown that prior direction of attention improves reaction speed and visual perception of target objects. According to the CCPP, spatial cue stimuli activate hypotheses about the characteristics of subsequent events, prepare motor responses, and adjust predictions in case of mismatch [32]. In addition, the influence of the probability of target stimuli matching the cue on event-related potential characteristics was revealed in the visual-auditory version of CCPP for mentally healthy individuals (50, 64/68 and 86/88% valid trials [matches between cue and target stimulus] were used) [27, 33, 34]. However, the effects of the probabilistic organization of stimulus material on predictive coding processes in individuals with schizophrenia remain unexplored.

The study aimed at evaluating the effects of the probability of the events on event-related potentials in schizophrenia patients compared to healthy individuals.

METHODS

We published the preliminary results of this study in [35]. The article, which covers the results of a pilot study on this topic, provides an analysis of existing methods, describes the development and testing of a technique (stimulation, analysis algorithm, and ERP component selection). The results of the pilot study were employed in this research.

Study design

A cross-sectional comparative study was conducted.

Setting

The study was conducted at V. Serbsky National Medical Research Centre of Psychiatry and Narcology of the Ministry of Health of the Russian Federation (V. Serbsky National Medical Research Centre) (Moscow, Russia). The main group consisted of patients with schizophrenia who underwent forensic psychiatric evaluation at V. Serbsky National Medical Research Centre from November 2022 to March 2023. The control group included employees of V. Serbsky National Medical Research Centre and acquaintances of the investigators.

Participants

Inclusion criteria: The main group included male patients with normal or corrected vision, without signs of acute psychotic state (to ensure quality recording of electroencephalogram [EEG]), who had not received pharmacotherapy (for at least 7 days before inclusion in the study), without a history of neuroinfectious diseases and concomitant mental disorders (according to medical documentation and examination findings at the time of assessment). All patients underwent forensic psychiatric evaluation at V. Serbsky National Medical Research Centre and were diagnosed with schizophrenia by their attending physicians (F20 according to the International Classification of Diseases, 10th Revision).

The control group consisted of male individuals without neurological or psychiatric disorders (according to self-reported data). This group was selected by frequency matching, so that the age distribution would be similar to that of the main group.

Non-inclusion criteria: Individuals were not included in the study if they were unable to follow the study protocol (severe cognitive impairment that made it difficult to understand the instructions for conducting the electrophysiological study), if they had been diagnosed with alcohol or drug dependence (the presence of the disease was established by the attending physician at V. Serbsky National Medical Research Centre), or were left-handed. The dominant hand was determined just before the neurophysiological study based on the results of a questionnaire (which hand the patient uses for writing, drawing, holding a toothbrush, scissors, a match when lighting it, a spoon when stirring liquids) and motor tests for the dominant hand (applause, interlocked fingers).

Exclusion criteria: Participants with unsatisfactory EEG quality were excluded from further analysis.

Electroencephalography

Registration

The recording of the brain's electrical activity was performed using a Neuroscan Synamps System (Compumedics, USA) from 19 channels according to the standard 10–20 system. Reference electrodes were placed on the earlobes, and a ground electrode was located at the Fpz position. The EEG signal was recorded with a sampling rate of 1000 Hz and a bandwidth of 0–500 Hz.

The study was conducted in a darkened and electrically shielded room. During the investigation, which lasted approximately 30 minutes, the participants were seated in a chair with soft upholstery, a high headrest, and armrests, which allowed them to maintain a stable posture and minimized discomfort.

The recordings were carried out by the study authors, who had over 15 years of experience in EEG recording.

Study protocol

To study the features of anticipation, a visual stimulation paradigm based on CCPP was applied, according to which two probability conditions were proposed [32]. The choice of visual stimulation is attributable to the fact that predictive coding processes have been most thoroughly studied in the visual modality. The STIM2 stimulator (Compumedics Neuroscan, USA) was used for presenting visual stimuli. The stimuli were displayed on a monitor (19" diagonal, screen resolution 1280x1024), with the center of the screen adjusted vertically to align with the participants' eye level and positioned at a distance of approximately 60 cm from their eyes. The presentation protocol had been previously tested [35]. All participants were given the same instructions and were asked to perform a saccadic task — shifting their gaze to the target stimulus [32].

Before the main session, participants had completed a brief training session to become familiar with the study procedure. In case of incorrect task performance, participants were re-instructed. The quality of instruction comprehension and the process of performing the study protocol were monitored using electrooculography with Ag/AgCl skin electrodes placed at the lateral corners of both eyes by monitoring correct eye movements in response to the stimuli. In addition, the electrooculography channels were used to determine the characteristics of behavioral responses (saccades): the latency period of correct saccades was identified using a peak detection algorithm that exceeded a predefined threshold for random fluctuations.

Based on the direction of the saccades, the percentage of correct and incorrect task performances was calculated.

The study consisted of five consecutive blocks, each containing 45 trials, with a one-minute break between blocks. Each trial consisted of four sequentially presented stimulus types: (1) green or yellow preparatory stimulus appeared in the center of the screen for 200 ms; (2) white central fixation stimulus appeared 600–800 ms after the disappearance of the preparatory stimulus, at the same location, and remained for 900–1100 ms; (3) white cue stimulus appeared immediately after the disappearance of the central fixation stimulus, positioned 5 cm to the left or right of it, and displayed for 150 ms; (4) green target stimulus appeared 1300–1500 ms after the disappearance of the cue stimulus, located 3 cm from the edge of the monitor, and shown for 1000 ms (Figure 1). Each trial began with the participant pressing a button, which initiated the sequence of four stimuli. Participants were instructed to maintain their gaze fixed at the center of the screen during the presentation of the first three stimuli. They were also instructed to shift their gaze to the target stimulus as quickly as possible once it appeared. After each trial, participants were required to return their gaze to the center of the screen.

The number of trials was chosen so that each type of stimulus was presented the necessary and sufficient number of times to average the ERP, taking into account possible artifacts [36]. Breaks between blocks were included to minimize fatigue.

Two experimental schemes were used in the study. In the first scheme, the preparatory stimulus was green and indicated to the participants (according to the instructions) that the target stimulus would appear on the same side as the cue stimulus with an 80% probability. In the second scheme, the preparatory stimulus was yellow and indicated that the probability of the cue and target stimuli had a 50% probability of appearing on the same side. A target stimulus presented on the same side as the cue stimulus will hereafter be referred to as a standard stimulus, while one presented on the opposite side will be referred to as a deviant stimulus. Thus, the target stimulus was presented under four conditions: 1) match with the cue stimulus at 80% probability (standard stimulus in the 80% condition) — 91 trials; 2) mismatch with the cue stimulus at

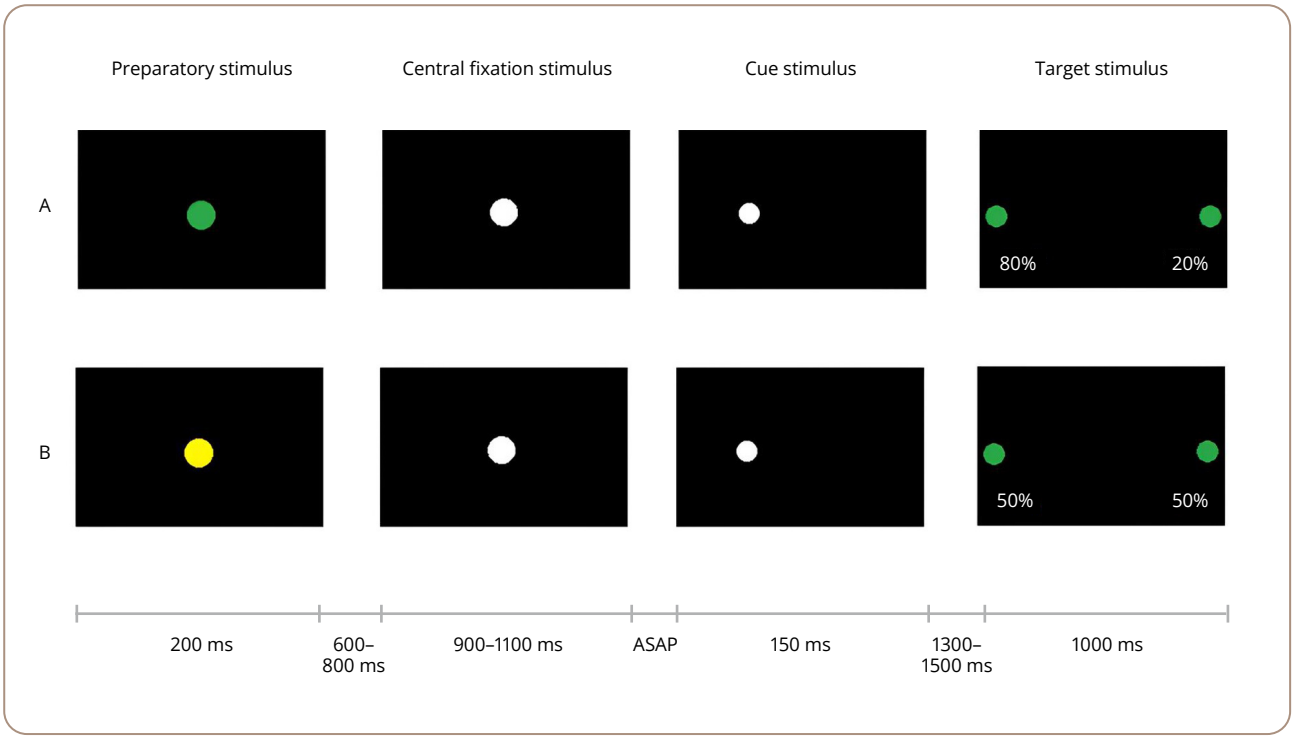

Figure 1. Visual stimuli presentation scheme.

Note: ASAP — as soon as possible; A — the target stimulus appears on the same side as the cue stimulus in 80% of the cases; B — the target stimulus appears on the same side as the cue stimulus in 50% of the cases.

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80% probability (deviant stimulus in the 80% condition) — 25 trials; 3) match with the cue stimulus at 50% probability (standard stimulus in the 50% condition) — 54 trials; and 4) mismatch with the cue stimulus at 50% probability (deviant stimulus in the 50% condition) — 55 trials.

The sequence of trials was predetermined and consistent for all participants. To avoid sequence effects, the order was randomized prior to the initiation of the study. The randomization was achieved by employing a sequence of random numbers generated using the Python programming language, in accordance with the specified stimulus probabilities. Given that the stimuli were generated probabilistically, the final distribution of stimuli was approximate and might not have exactly matched the predefined probabilities.

Record preprocessing

The EEG recordings were filtered within the range of 0 to 30 Hz. Oculomotor artifacts were removed using independent component analysis. After that, the records were visually inspected for the presence of artifacts. The CNV was isolated by epoching EEG data from −1 to 0 seconds, relative to the onset of regular saccades (latency >120 ms). A baseline was defined from −1 to −0.9 seconds, and the epochs were then averaged for each participant. Then, the EEG recordings were converted to a time constant of 5 seconds to obtain slow potentials. The transformation procedure is based on the fact that the cutoff frequency of analogue filters corresponds to a transmission coefficient drop of only −3 dB, meaning that only a portion of the slow activity passes through the filter. However, the part of the activity that did not pass through the filter's stopband can be restored, except for the direct current component [37]. The CNV analysis was conducted in the early (900–600 ms before the target stimulus) and late (300–0 ms before the target stimulus) intervals, for which average amplitude values were obtained.

For post-stimulus ERP, the records were segmented in the range from −0.2 to 0.7 seconds relative to the target stimulus, with a baseline correction applied in the range from −0.2 to 0 seconds, and then averaged for each study participant. For the ERP components extraction, filtering was performed in the 1–7 Hz range to eliminate slow-wave artifacts and alpha rhythm interference. For the purpose of further analysis and to minimize data redundancy, 9 key channels were selected. These channels cover the regions responsible for the generation of the analyzed potentials and are least susceptible to oculographic and myographic artifacts (F3, F4, Fz, C3, C4, Cz, P3, P4, Pz). The P3 component was identified on these channels as the maximum positive peak within the 220–400 ms interval (for latency analysis, see Table S1 in the Supplementary). The P3 amplitude was evaluated as the peak-to-peak amplitude from the preceding negative peak within the 100–300 ms interval, which was identified visually (see Figure 2). For the MMN analysis, the mean amplitude was extracted within a ±50 ms window centered on the peak negative amplitude in the 100–250 ms time range after subtracting the ERP elicited by the standard stimulus from that elicited by the deviant stimulus. Data were preprocessed by one of the authors of the study (Rabinovich EI).

Statistical analysis

Data analysis was performed in the software environment for the Python programming language (EEG processing, multiple-comparison correction) and with the Jamovi statistical software package, version 2.3.31 (normality testing, ANOVA, and t-tests). The visualization of ERP and the construction of topographic maps were carried out using the MNE library for the Python programming language [38]. The Shapiro–Wilk test was applied to assess

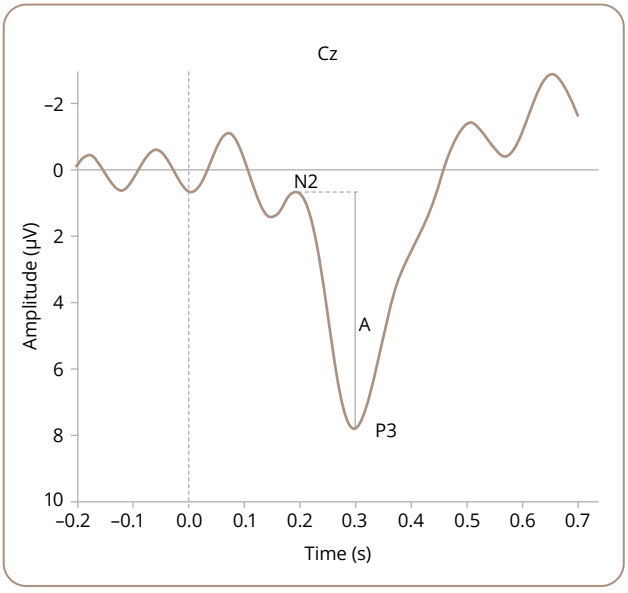

Figure 2. The event-related potential waveform recorded on the Cz electrode.

Note: The method for measuring the amplitude (A) of the P3 component is indicated. N2 — the preceding negative peak. Vertical dashed line — the time of stimulus presentation.

Source: Rabinovich, Telesheva, 2025.

the distribution of the quantitative variables (there were no deviations from the normal distribution, $p>0.05$ in all cases). In this connection, the quantitative variables were described using the arithmetic mean (standard deviation).

The amplitudes of ERP components were compared using repeated measures analysis of variance with the between-subjects factor "group" ($n=2$, schizophrenia and control groups). In the analysis of CNV, P3, and MMN, the following within-subject factors were taken into account: the probability of the cue and target stimuli matching ($n=2$: 50% and 80%) and electrode location ($n=3$: frontal, central, and parietal). Additionally, when analyzing the CNV, the analysis interval was taken into account ($n=2$: early [900–600 ms before the peripheral stimulus] and late [300–0 ms before the peripheral stimulus]), while for the P3 analysis, the match between the cue and target stimuli was taken into account ($n=2$: standard and deviant stimuli). The selection of the listed factors is based on theoretical premises and the methodology employed in the study of anticipation.

Post hoc analysis was conducted using paired Student's t-tests and independent Student's t-tests. Multiple-comparison correction was performed by calculating the False Discovery Rate (FDR).

Ethical approval

The study was approved by the Ethics Committee of V. Serbsky National Medical Research Centre (Minutes No. 3 6/3 dated December 6, 2021). All participants signed an informed consent form for participation in the study.

RESULTS

Participants

During the study period, 20 patients with schizophrenia undergoing a forensic psychiatric evaluation at V. Serbsky National Medical Research Centre met the inclusion criteria. All patients were invited to participate in the study, of whom two declined to participate; 18 patients were included in the study and completed the protocol in full. The data from one patient was excluded from the CNV analysis due to poor EEG quality (a large number of slow-wave artifacts).

Twenty-two mentally healthy individuals were invited to join the control group; all of them were included in the study and completed the protocol in full. However, one EEG record was completely excluded from the analysis due to the participant's functional state (drowsiness), and another was excluded due to a large number of artifacts. The control group comprised 20 people.

Characteristics of the study groups

The mean age of the subjects in the control group and the patient group was 30.4 (6.5) years and 33.3 (6.3) years, respectively ($p=0.121$). Sixteen patients were diagnosed with paranoid schizophrenia (F20.0), one with hebephrenic schizophrenia (F20.1), and one with another form of schizophrenia (F20.8). The duration of the disease exceeded 5 years in 15 patients and was less than 5 years in the rest of the patients. In the main group, Positive and Negative Syndrome Scale (PANSS) scores averaged 16.3 (5.8) for positive symptoms, 18.4 (6.1) for negative symptoms, and 34.4 (8.3) for general psychopathological symptoms.

Main results

The performance results were analyzed using saccade characteristics under different stimulus presentation conditions. Table 1 shows the latencies of regular saccades (latency ≥120 ms) toward the target stimulus, the percentage of anticipatory saccades (latency <0 ms) and express saccades (latency ≥0 ms, <120 ms), and the percentage of error saccades, defined as gaze shifts to the direction opposite to the cue stimulus. The latent periods of regular saccades in the study groups were comparable. The percentage of errors when responding to the standard stimuli was higher in schizophrenia patients. Schizophrenia patients also showed a higher overall percentage of anticipatory and express saccades compared to the control group under conditions of 50% stimulus matching probability, although the differences did not reach the level of statistical significance (see Table 1). Within-group analysis revealed that, in the control group, saccade latency to the standard stimulus in the 80% condition was shorter than that to the deviant stimulus ($t=-3.94$, $p=0.002$). No differences were revealed in the latencies of saccades to the standard and deviant stimuli in the 50% condition ($t=-0.53$, $p=0.599$). The highest number of saccadic errors was observed in response to deviant stimuli under the 80% condition, compared to other conditions ($p<0.01$ in all cases). At the same time, the 80% matching condition produced the highest number of anticipatory and express saccades. In schizophrenia patients, no statistically significant differences were found across conditions in saccade latency, the percentage of error saccades, or the percentage of anticipatory and express saccades. A repeated-measures ANOVA in the control group revealed a significant probability and matching interaction affecting latency ($F=12.74$, $p=0.002$, partial $\eta^2=0.401$) and

Table 1. Parameters of saccadic eye movements in control group and schizophrenia patients

Parameters	Control group (*n*=20)	Schizophrenia patients (*n*=18)	t	*p*
Latency of regular saccadic eye movements (ms)				
Standard 50%	263.1 (43.3)	273.7 (51.7)	−0.67	0.603
Deviant 50%	264.1 (40.3)	280.1 (61.0)	−0.92	0.479
Standard 80%	247.8 (40.1)	266.4 (55.2)	−1.17	0.376
Deviant 80%	270.7 (43.6)	281.5 (64.0)	−0.60	0.603
Errors in saccadic eye movements (%)				
Standard 50%	2.2 (3.6)	10.1 (11.3)	−2.99	0.031
Deviant 50%	4.1 (8.2)	7.7 (8.3)	−1.31	0.376
Standard 80%	1.5 (1.3)	7.4 (8.2)	−3.17	0.031
Deviant 80%	10.3 (7.2)	5.5 (5.9)	2.01	0.156
Anticipatory and express saccades (%)				
Standard 50%	3.7 (6.2)	10.8 (10.5)	−2.56	0.060
Deviant 50%	4.5 (6.5)	8.9 (8.5)	−1.78	0.202
Standard 80%	7.1 (8.0)	10.7 (9.6)	−1.21	0.376
Deviant 80%	8.3 (7.5)	7.6 (6.8)	0.25	0.803

Note: The quantitative variables were described using the arithmetic mean (standard deviation).

error rate (F=12.58, p=0.002, partial η^2=0.398); a significant main effect of probability on the proportion of anticipatory and express saccades (F=11.40, p=0.003, partial η^2=0.375). The schizophrenia group demonstrated a link between the matching factor and the regular saccade latency (F=5.70, p=0.030, partial η^2=0.276).

Subsequent to the comparison of CNV values between groups using analysis of variance, no significant differences were identified. The control group demonstrated a statistically significant influence of the probability factor (F=9.26, p=0.009, partial η^2=0.398), as well as a significant interaction of the probability and interval factors (F=7.60, p=0.015, partial η^2=0.352). *Post hoc* analysis revealed no statistically significant differences in the early CNV interval between the 50% and 80% probability conditions (t=1.70, p=0.111). Significant differences were observed in the control group during the late CNV interval in two conditions (t=3.32, p=0.006). The mean amplitude at 50% probability was −6.35 μV; at 80% probability was −8.46 μV.

The analysis of MMN showed the significant effect of the intergroup factor (F=5.53, p=0.025, partial η^2=0.144). In the control group, differences between the conditions of 50% and 80% stimulus matching probabilities were identified in the parietal (t=3.521, p=0.022) and central (t=2.627, p=0.045) regions. The mean amplitude of MMN for all analyzed leads in the 50% and 80% conditions was −0.17 μV and −1.58 μV, respectively (t=3.09, p=0.007). The schizophrenia group demonstrated no differences between the 50% and 80% probability conditions. A decrease in the MMN was more pronounced in the frontal and parietal regions (when compared to the control group in the 80% probability condition [p=0.038 and p=0.019, respectively]). The mean MMN amplitudes in the 80% condition in the schizophrenia group on the frontal and parietal electrodes were 0.12 μV and 0.43 μV, respectively.

The analysis of P3 amplitudes revealed differences between the groups in the interaction between probability and matching factors (F=4.39, p=0.044, partial η^2=0.117).

The analysis of P3 amplitudes in the control group demonstrated that the most pronounced differences between the amplitudes to the standard and deviant stimuli were observed in the frontal (t=−4.93, p<0.001) and central (t=−5.13, p<0.001) regions. Moreover, in the control group the amplitude to deviant stimuli was significantly higher than that to standard stimuli under both the 50% (t=−3.02, p=0.009) and 80% (t=−5.44, p<0.001) probability of stimulus side matching. In the schizophrenia group, no increase in amplitude to deviant stimuli relative to standard stimuli was observed in the 80% probability of stimulus side congruence. In the 50% condition, the amplitude

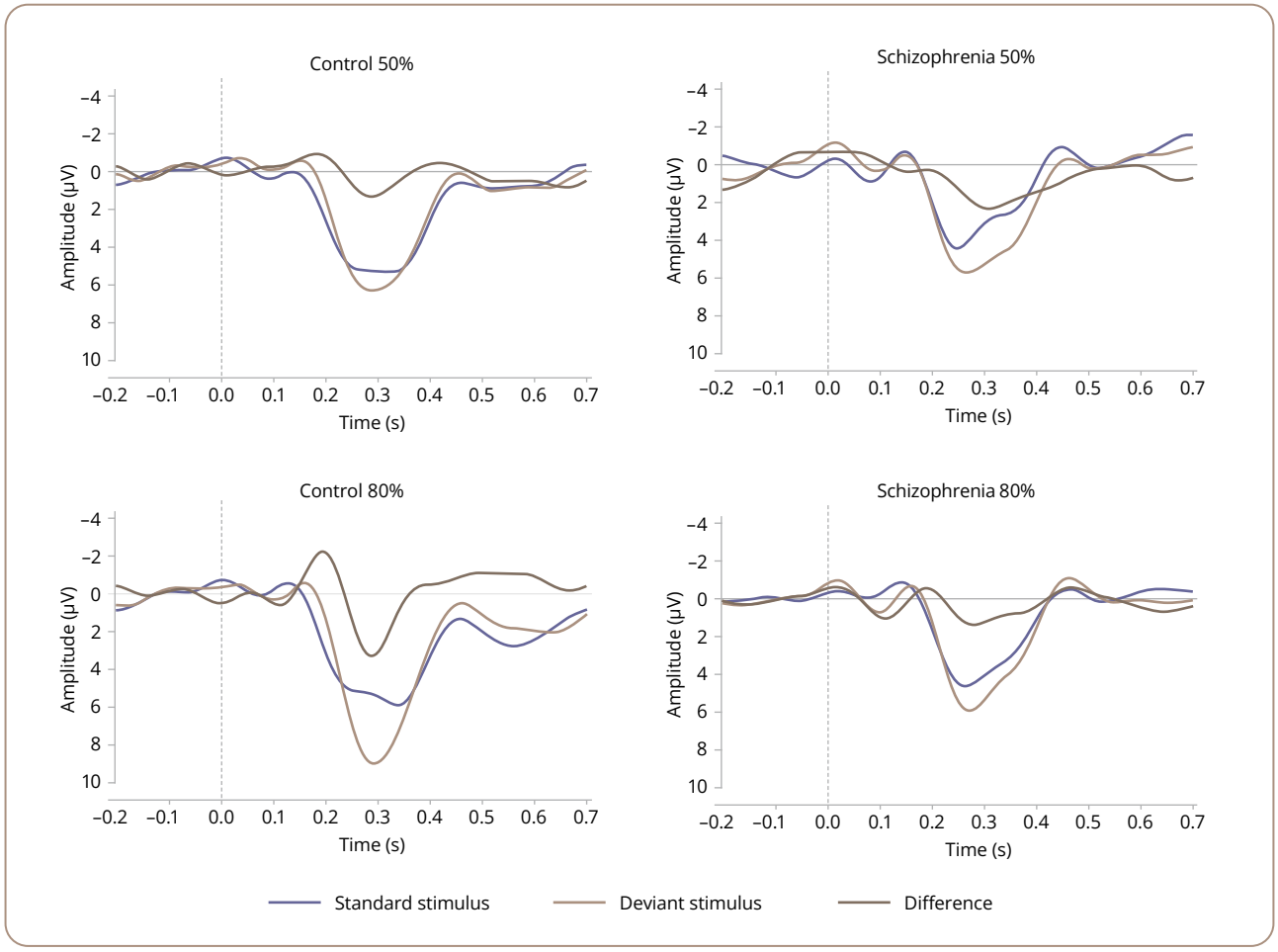

Figure 3. Event-related potentials (grand averaged for the groups) to the target stimuli on the Cz electrode.

Note: The dashed line marks the moment of stimulus presentation.

Source: Rabinovich, Telesheva, 2025.

to the deviant stimulus was higher than in the standard stimulus (t=−2.32, *p*=0.034). The averaged ERPs for the two groups at the Cz electrode are presented in Figure 3.

Additional results of the study

Analysis of the ERPs in individuals with schizophrenia showed variations in CNV amplitudes across the two conditions in contrast to the control group, where such variations were not observed. Accordingly, two patient subgroups were identified: the first subgroup included 10 patients (59%) whose CNV amplitude was higher in the 50% condition than in the 80% condition, or showed no difference between the two conditions; the second subgroup included 7 patients (41%) whose CNV amplitude was higher in the 80% condition. Thus, among patients in the first subgroup there was no effect (or a distorted effect) of probability on the CNV amplitude, whereas in the second subgroup a higher event probability produced a larger CNV amplitude. All subjects in the control group satisfied the criterion of the second subgroup (the CNV amplitude was higher in the 80% condition versus the 50% condition).

A subsequent comparison of the first subgroup with the control group revealed a significant differences between the groups in the interaction between probability and interval factors (F=5.10, *p*=0.034, partial η^2=0.182). Significant differences between these groups were observed in the late interval under the 80% condition (t=2.83, *p*=0.019). Within the first subgroup, no factors were found to influence CNV amplitude. There were no differences between the probabilities in either early (t=0.093, *p*=0,928) or late (t=−0.40, *p*=0.834) intervals. The results of the second subgroup did not show any significant differences from the control group. In the second subgroup there were

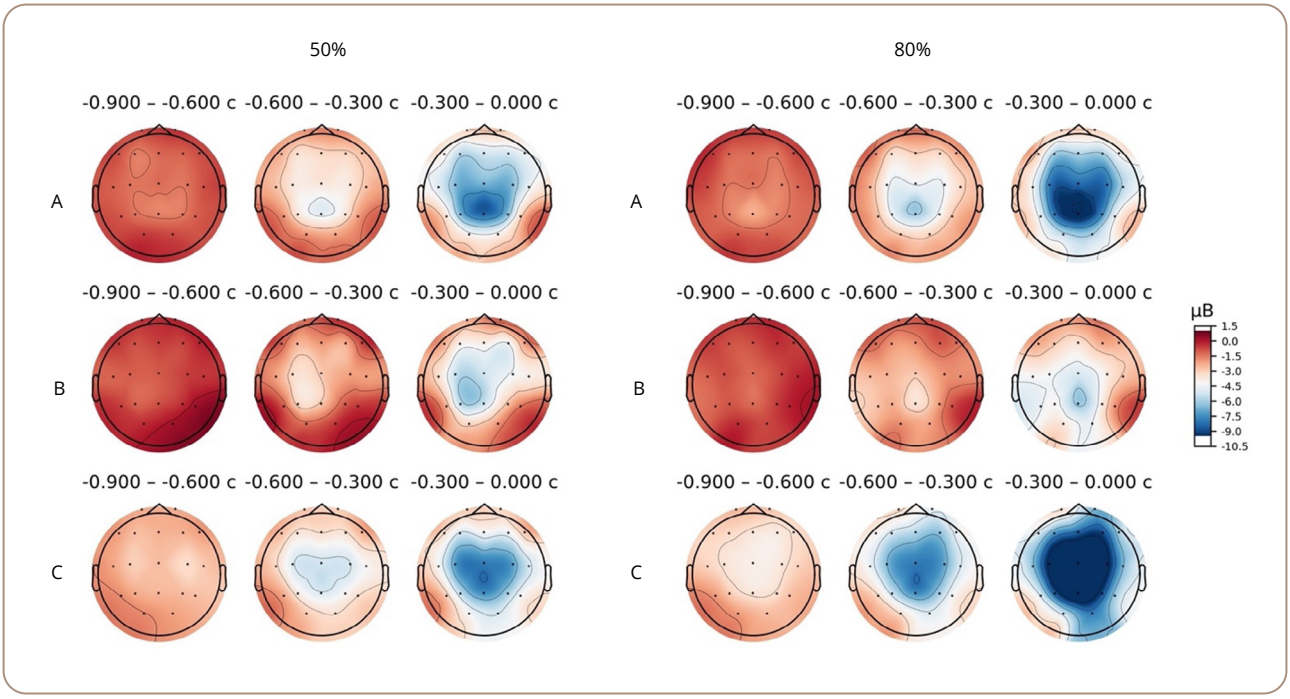

Figure 4. Topographic maps of the contingent negative variation.

Note: The left column represents the 50% probability condition, and the right column represents the 80% probability condition. Averaged amplitudes for the specified time intervals are shown. A — control group; B — first schizophrenia subgroup (CNV amplitude was higher in the 50% condition than in the 80% condition, or showed no difference between the two conditions); C — second schizophrenia subgroup (CNV amplitude was higher in the 80% condition versus the 50% condition).

Source: Rabinovich, Telesheva, 2025.

significant differences between probabilities in the late interval: the mean amplitude in the 50% and 80% conditions was −5.35 μV and −9.88 μV, respectively (t=3.34, *p*=0.024).

There were no significant differences in the MMN and P3 amplitudes between the first and second subgroups.

Topographic maps of the CNV for the control group, the first subgroup, and the second subgroup of individuals with schizophrenia are shown in Figure 4.

DISCUSSION

Key results

The study demonstrated neurophysiological features of anticipation in schizophrenia patients: the patients showed a higher error rate in response to standard stimuli and a greater proportion of anticipatory and express saccades in the 50% matching probability condition compared to mentally healthy individuals. There were no significant differences in the CNV characteristics between the groups. However, schizophrenia patients showed differences in MMN and P3 component amplitudes from the control group. Specifically, no substantial differences in the MMN amplitude were detected between the 50% and 80% stimulus congruence probability conditions within the schizophrenia group. In contrast, these differences were found to be statistically significant in the control group. Under the 80% stimulus congruence probability condition, the schizophrenia group lacked the characteristic increase in P3 amplitude in response to deviant stimuli that was observed in the control group. Both behavioral and neurophysiological responses in mentally healthy individuals depended on the probability and stimulus type. At an 80% probability, saccade latency was found to be shorter, the number of anticipatory and express saccades (and the deviant stimulus error rate) increased, and the late CNV phase, MMN amplitude, and P3 amplitude all differed between the 50% and 80% conditions, with the largest amplitude appearing for the deviant stimulus in the 80% condition. Schizophrenia patients showed no differentiation of behavioral or neurophysiological responses depending on the conditions. The saccade latency did not vary when the probability changes, and the overall number of saccade errors (anticipatory and

express saccades) was higher than in mentally healthy individuals. There were no changes in the CNV, MMN, and P3 amplitudes between the conditions.

Interpretation

The study showed that there is an absence of influence of the probability in predictive processing in schizophrenia patients. Analysis of saccade characteristics revealed impairment in assessing stimulus probability. In the control group, presenting the standard stimulus under the 80% matching probability condition led to an the expectation of its occurrence in a specific location. This expectation resulted in a reduction in the latency of regular saccades and an increase in the number of anticipatory and express saccades. With deviant stimulus presentation in the 80% probability range, the error response rate increased. This reflects the ability of the patient to form robust predictions based on probabilistic information. The latent period of regular saccades in schizophrenia patients did not differ from that in mentally healthy individuals, consistent with earlier published studies [39]. However, no differences between conditions were observed in patients, which may indicate an inability to form reliable predictions regarding the appearance of stimuli under different probabilities. At the same time, patients with schizophrenia generally exhibit a higher number of errors, which may be linked to an increased incidence of express saccades due to the dysfunction of the prefrontal cortex and impaired inhibitory control, consistent with findings from other studies [30, 40].

In healthy individuals, changes in predictive processes are associated with a preliminary activation of neuronal structures and are reflected in CNV characteristics [26]. Mentally healthy individuals showed an increase in the CNV amplitude under the 80% stimulus matching probability compared to the 50% probability. This is consistent with the literature indicating that an informative signal stimulus elicits a higher CNV amplitude compared to a neutral stimulus [41]. Thus, top-down probabilistic predictions facilitate the optimization of stimulus processing and motor response preparation [41, 42]. In mentally healthy participants, the maximum CNV amplitude shifted over time from parietal sites in the early phase to central-parietal and frontal regions in the late phase. The gradual increase in the CNV amplitude in these regions may reflect anticipatory processes linked to visuospatial attention that facilitate the selection of relevant stimuli for subsequent processing [43].

Additional analysis of the CNV in patients with schizophrenia revealed divergent changes across the two conditions. Particularly, half of patients demonstrated an increase in the CNV amplitude when the stimulus matching probability increased. The other half did not show such a trend. Accordingly, two principal patterns of predictive impairment can be distinguished in schizophrenia patients: one subgroup relies more on prior predictions than on sensory data, while the other relies more on sensory information than on top-down influences [44, 45]. Overall, our results demonstrate the heterogeneity of disorders in predictive processes in schizophrenia patients [46].

Many studies have considered the MMN and the P3 component to reflect the response to expectation violations [12, 23, 47]. Our study showed that, in mentally healthy individuals, the MMN amplitude is higher under the 80% probability condition compared to the 50% condition. This may which may reflect a higher generation of prediction errors when deviations occur in a context of high stimulus-congruence probability. The MMN amplitude in schizophrenia patients was lower than in the control group, which is consistent with the results of studies demonstrating a MMN decrease in schizophrenia patients [8, 12, 48]. Our data showed that schizophrenia patients had the lowest MMN amplitude in the frontal and parietal leads. This is supported by research findings indicating that the automatic response to a visual deviant stimulus is modulated by the fronto-occipital network, and that the lowest amplitude of visual MMN in schizophrenia patients is observed in the frontal and occipitoparietal regions [49, 50].

Based on the results obtained with mentally healthy individuals, it can be concluded that a higher probability of stimulus appearance increases the contribution of predictive and top-down processes to perception and motor-response preparation [4]. A stimulus that does not match the prediction leads to a prediction error and serves as an informative signal that updates further predictions [8, 12]. It is proposed that the reduced MMN amplitude in schizophrenia patients is associated with impaired predictive processes and probability assessment, such that each stimulus fails to conform to the learned sequence and triggers a prediction error [4]. The greatest reduction in amplitude in the frontal and parietal regions may indicate a dysfunctional integration of brain networks, which manifests as in impaired descending modulation of the parietal-occipital regions by the prefrontal cortex [51].

The analysis of the P3 component in mentally healthy individuals showed an increased amplitude to the deviant stimuli under the 80% matching condition. Schizophrenia patients showed an increase in the amplitude to the deviant stimuli in the 50% probability condition and a decrease in the amplitude to the deviant stimuli in the 80% condition, which reflects the aberrant probability assessment [52, 53]. This supports the hypothesis that prediction errors in schizophrenia patients are generated in response to stimuli that are less significant for predictive processes (e.g., a stimulus with a 50% probability) and are linked to an impaired ability to identify significant stimuli (aberrant salience) [49, 54]. The paradigm employing deviant stimuli with equal probability to standard stimuli may represent a novel approach for evaluating impairment in probabilistic prediction and anticipation in schizophrenia patients.

Limitations

These study results cannot be extrapolated to all cases of schizophrenia, since the patients included in this study were not experiencing an acute psychotic episode and displayed minimal manifestations of positive symptoms.

Another limitation is the small sample size, which increases the risk of type II errors and limits the ability to account for within-group heterogeneity.

Non-standard frequency ranges were used for filtering when extracting ERP peaks, which impedes comparison of the results with other investigations. This was due to an attempt to identify clear peaks not affected by noises from the alpha rhythms (without any significant amplitude distortions). Moreover, it appeared that the various filters had not significantly distorted the P3 component [55].

Our study did not aim to evaluate the connection between the neurophysiological parameters of anticipation and clinical manifestations of schizophrenia, or the effects of the latter on the key findings of this study.

CONCLUSION

The results of our investigation indicate that there are significant differences in ERP reflecting anticipation and information processing between mentally healthy individuals and patients with schizophrenia. These results align with existing theories about disturbances in prediction and error detection processes in schizophrenia. In mentally healthy individuals, the probability was associated with the CNV amplitude, MMN, and P3 characteristics. This suggests an effective use of probabilistic information in the prediction and preparation of the motor response and is confirmed in the saccade characteristics. The lack of a definite influence of the probability factor on the CNV, MMN, and P3 amplitudes in patients with schizophrenia confirms the impairment of predictive processes in these individuals.

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Supplementary data

Supplementary material to this article can be found in the online version:
Table S1: 10.17816/CP15558-145305

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