VILNIUS UNIVERSITY

Kastytis Dapšys

STUDY OF PSYCHIATRIC DISORDERS AND EVALUATION OF THEIR TREATMENT USING METHOD OF AUDITORY EVOKED POTENTIAL P300

Summary of doctoral dissertation
Biomedical sciences, Biophysics (02 B)

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VILNIAUS UNIVERSITETAS

Kastytis Dapšys

PSICHIKOS SUTRIKIMŲ TYRIMAS IR JŲ GYDYMO ĮVERTINIMAS KLAUSOS SUKELTO POTENCIALO P300 METODU

Daktaro disertacija

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CONTENTS

ABBREVIATIONS

DSM IV	- diagnostic and statistical manual of psychiatric disorders, 4th edition
ECT	- electroconvulsive therapy
EEG	- electroencephalography
ERP	- event-related potential
HAMD	- Hamilton depression rating scale
ICD-10	- international classification of diseases, 10th revision
MADRS	- Montgomery-Åsberg depression rating scale
MGT	- metaglossotherapy
N2L	- N2 latency
P3A	- P300 amplitude
P3L	- P300 latency
PANSS	- positive and negative syndrome scale
PSI	- postictal suppression index
RT	- recognition time
RVPH	- Republican Vilnius Psychiatric Hospital
SEI	- seizure energy index
WAIS	- Wechsler adult intelligence scale

1. INTRODUCTION

Persistent neurocognitive dysfunction represents one of the major predictors of chronic disability and impaired long-term outcome in different psychiatric disorders (Harvey et al., 1990; Kay and Murrill, 1990; Green et al., 2000). This is especially evident in the case of schizophrenia spectrum disorders. There is number of methods to treat psychiatric symptoms, however their influence on the cognitive functions of psychiatric patients is not sufficiently studied and poorly understood. It is also a problem to correctly measure and objectively evaluate cognitive processes. Many tests were created to evaluate cognition of psychiatric patients, but many of them are not available in Lithuania due to numerous reasons, such as lack of translated and approbated tests. However there is a method, which may help to solve at least the part of the problem – the method of event-related potentials (ERP). ERPs can be used to study some cognitive functions. Almost from the beginning of their development they were applied to study disturbances of cognition in psychiatric disorders. ERPs are noninvasive, objective and relatively inexpensive (Morihisa, 1989; Kuperberg, 2004; Luck, 2005). This method is safe and harmless so it is possible to record them several times a day. This makes them suitable to follow the changes of cognitive processes induced by psychoactive drugs or other therapeutic procedures. However the nature of ERPs and their abnormalities in psychiatric disorders is not clear enough. There is also no certainty which parameters of ERPs are most informative and with which elementary cognitive processes they are related (Luck, 2005). The influence of different therapeutic techniques on the ERPs is still fully unexplored. Among different types of ERPs the P300 potential stands apart as one of the first explored (Sutton et al., 1965) and best researched (Duncan et al., 2009). Now it is thought, that P300 ERP reflects processes of active attention and update of operational memory (Donchin and Coles, 1988). The changes of parameters of P300 in patients with schizophrenia (Ford et al. 1994; Juckel et al., 1996; Bramon et al., 2004; Molina et al., 2005; Galderisi et al., 2009) shows, that this is sensitive indicator of disturbed cognitive functions.

Pharmacological treatment is the most popular method of treatment of psychiatric disorders. Now there are a great number of neuroleptic drugs however their action, especially effect on the cognition, is not properly studied. For example, new generation (atypical) antipsychotics, such as clozapine, risperidone, olanzapine,

quetiapine, which were developed to treat the symptoms of schizophrenia, effectively diminishes the symptoms of psychosis (Velligan et al., 2003; Yang-Tae and Byung-Jo, 2004) and have fewer side effects then their predecessors – first generation antipsychotics, however their influence on the cognitive functions of the patients is limited and unsatisfactory (Carter, 2005; Goldberg et al., 2007; Keefe et al., 2007). Their action on the brain neuronal processes related to cognition is also obscure. *Therefore the study of the influence of atypical antipsychotics on the parameters of P300 potential is very important in order to receive new information about the action of new antipsychotic medication on the information processing in the brain.*

Along with pharmacological treatment, especially when the patients are treatment resistant, other methods can be applied, such as electroconvulsive therapy (ECT). When impulsive electric current is applied to the brain the generalized seizure is evoked (Abrams, 2002). Under its influence different physiological changes are taking place in the brain neurons and these changes induce positive therapeutic effect (Grover et al., 2005). Practice shows that ECT is safe and effective method of treatment. It is even more so when modified method of ECT is used – the patient receives anesthetics and myorelaxants and so the convulsive seizures are avoided. ECT procedures in Republican Vilnius psychiatric hospital are carried out using ECT machine "Thymatron Dx". It also records one channel of EEG, from which a number of seizure quality parameters can be calculated (Abrams and Swartz, 1994). The mechanisms of therapeutic ECT action are still not fully clear as are the causes of infrequent negative side effects, such as memory impairment (Ingram et al., 2008). *Influence of ECT on the cognitive functions of the psychiatric patients is not studied enough. There is also lack of data about relation of ECT procedure quality parameters and parameters of event-related potentials.*

As was already mentioned in the case of schizophrenia spectrum disorders the effect of antipsychotics on the cognitive functions is unsatisfactory, therefore other means are searched for to address this problem. One of the ways is to develop new medication, which will specifically enhance cognition of schizophrenic patients. The necessity of this kind of neuroleptic drugs is acknowledged (Goldberg, 2007), but this way is time consuming and expensive. There is, however, a group of methods which are called "cognitive remediation". They are based on different exercises or computerized tests and games, devoted to enhance different cognitive functions (Hogarty et al., 2004;

Kurtz et al., 2007; Hodge et al., 2008). One of the most interesting methods, which may be attributed to this group, is a method called "metaglossotherapy" (Matulis, 1974). It is based on the teaching of schizophrenia patients a new, earlier unknown for them, language. It is thought that learning a new language can help the patients to reconstruct the reality anew, to formulate realistic, "normal" concepts using new linguistic constructions. *The influence of metaglossotherapy on the cognitive functions of schizophrenic patients was not studied at all and this is the first attempt.*

1.1. Aim of the work and its objectives

The main aim of the work was to evaluate the influence of atypical antipsychotics risperidone and quetiapine and such nonpharmacological methods as electroconvulsive therapy and metaglossotherapy on the changes of information processing in the auditory system using event-related potential P300 recording and analysis method.

Main objectives of the study were:

1. To study the influence of antipsychotic risperidone on the parameters of P300 potential of patients with schizophrenia spectrum disorders. To compare the data of the group of patients with the group of healthy controls, in order to evaluate the level of disturbance of cognitive functions. To find the correlation between P300 parameters and values of clinical symptoms measured using clinical tests.
2. To study the influence of antipsychotic quetiapine on the parameters of P300 potential of patients with schizophrenia spectrum disorders. To compare the data of the group of patients with the group of healthy controls, in order to evaluate the level of disturbance of cognitive functions. To find the correlation between P300 parameters and values of clinical symptoms measured using clinical tests.
3. To evaluate the changes of cognitive functions of patients with mood disorders and patients with schizophrenia spectrum disorders under the influence of electroconvulsive therapy using event-related potential P300 recording and analysis method.
4. To evaluate the changes of information processing in the auditory system after metaglossotherapy and to find correlation between parameters of P300 potential and results of cognitive tests.

1.2. Actuality and scientific novelty

Scientific novelty:

1. For the first time in Lithuania there was the influence of antipsychotic risperidone on the parameters of P300 studied in two groups of patients – with schizophrenia disorder and depressive type schizoaffective disorder.
2. For the first time in Lithuania the effect of antipsychotic quetiapine on the cognition of the patients with depressive type schizoaffective disorder using method of P300 potential recording and analysis was studied.
3. For the first time in Lithuania the changes of parameters of P300 potential after the course of ECT were evaluated and correlation with the indices of ECT procedure was investigated. The aspects of diagnosis and age of the patients also were evaluated.
4. For the first time in the world the influence of metaglosotherapy on the auditory event-related potential P300 was studied and the correlation of parameters of P300 with results of cognitive psychological tests was searched for.

Practical value:

1. The principles of recording of event-related potentials were tested, introduced and successfully applied in Republican Vilnius Psychiatric Hospital (RVPH) and the methods of their analysis were also evaluated.
2. The practice of pharmacological studies of event-related potentials in RVPH was analyzed and necessary corrections were proposed.
3. The principals of ERP study investigating the effect of electroconvulsive therapy on cognitive functions of the psychiatric patients were introduced and applied.
4. The method of enhancement of cognitive functions of schizophrenia patients – metaglossotherapy – was tested and introduced.

Practical recommendations

1. The application of principals of “naturalistic study” when psychopharmacological research of event-related potentials is carried out in RVPH is proposed, because

the monotherapy with neuroleptics in daily clinical psychiatric praxis is rather exception than the rule.

2. The changes of ERP parameters may be possible indicators of therapeutic effect of ECT, therefore it is proposed to record P300 potential not only at the baseline and ater the full course of ECT, but also in a middle of the course (after 5 procedures or 2 weeks of therapy).
3. More attention must be paid for such parameter of ECT procedure quality as seizure energy index (SEI), because it correlates with ERP P300 parameter - recognition time of target stimulus.
4. It was shown that the age of the patients has influence on the changes of P300 potential so it is suggested to pay more attention to the settings of the energy of ECT impulse according to the age.
5. Collected data indicate that nonpharmacological methods may be more effective in enhancement of cognition of psychiatric patients, then drug therapies, therefore it makes sense to devote more efforts to introduce such methods into clinical practice of psychiatric in-patient institutions.
6. It was shown that auditory event-related potential P300 is a sensitive method of evaluation of cognitive functions so it is recommended to apply it more widely as well as for investigation of abnormalities of cognitive functions in psychiatric disorders as for study of influence on them of different therapeutic methods.
7. It is suggested in the studies of event-related potentials of psychiatric patients to use not only the scales of clinical symptoms measurement, but also carefully selected and adapted psychological methods of evaluation of cognitive functions.

1.3. Statements to be defended

1. The parameters of P300 potential – N2 latency, P300 latency, P300 amplitude and recognition time of target stimulus (RT) – are sensitive indicators of abnormalities of information processing in auditory system in the case of schizophrenia spectrum disorders.
2. More considerable positive influence on the event-related potential P300 had atypical antipsychotic quetiapine.

3. Nonpharmacological methods of treatment of psychiatric disorders are as effective as drug therapy with atypical antipsychotics in remediation of cognitive functions.

2. METHODS

For all studies the consent of Ethical committee of Republican Vilnius Psychiatric Hospital was received.

2.1. Studies of pharmacological therapy on auditory event-related potential P300.

Diagnoses were made by trained psychiatrists according to ICD-10 International (WHO, 1992). Patients with organic CNS pathology, history of alcohol or drug dependence were not included. Healthy subjects from control groups, which were selected for all studies, also had no recorded neurological or psychiatric disorders.

2.1.1. Subjects.

Study of antipsychotic risperidone. There were two groups of patients composed regarding their diagnosis – group of patients with schizophrenia (diagnoses, which indexes start with F20) and schizoaffective disorder, depressive type (F25.1). Schizophrenia group was comprised of 15 subjects – 3 female, 12 male patients. Average age was 30.1±11.2 years (from 18 up to 50 years). There were 11 patients in the group of schizoaffective disorder – 7 female, 4 male. Average age was 24.8±10.5 years (from 18 up to 51 year). Individual dosage of risperidone was 2-3 mg/day (2.2±0.5 mg). At the time of first pre-treatment P300 potential recording all patients were never treated with risperidone, at least 1 month did not received other antipsychotics and during course of treatment no additional antipsychotics were included. Two separate groups of age-matched healthy controls were composed. Characteristics of the subjects are presented in Table 2.1.

Table 2.1. Patients and healthy controls of risperidone therapy study

	Schizophrenia (F20) group	Control group 1	Schizoaffective (F25.1) group	Control group 2
Number of participants	15	15	11	11
Average age	30.1±11.2 years	31.0±10.4 years	24.8±10.5 years	24.5±4.8 years
Males	12	9	4	4
Females	3	6	7	7

Study of antipsychotic quetiapine. There were 10 patients in the group of quetiapine. Their average age was 40.1±10.8 years (9 females and 1 male). Oldest patient was 56 years old, youngest – 23. All patients had diagnosis of schizoaffective disorder, depressive type (F25.1). A control group of healthy controls of the similar age was composed. The average age of subjects in this group was 40.1±11.2 years (from 23 up to 56 years). There were 6 males and 4 females in the group.

Average individual dosage of quetiapinum was 470±140 mg/day. At the time of first pre-treatment P300 potential recording all patients were never treated with quetiapinum, at least 1 month did not received other antipsychotics and during course of treatment no additional antipsychotics were included.

2.1.2. Study design and data analysis.

In pharmacological therapy studies recordings of P300 potential were made 3 times: before therapy, after 2 and 4 weeks of therapy. Measurements of P300 at baseline were compared with data of healthy controls and measurements made in the course of drug treatment. All recordings were made in the morning between 9 and 12 a.m.

Clinical symptoms were measured using PANSS - Positive And Negative Syndrome Scale (Kay et al., 1987). PANSS measures were made by trained psychiatrists two times – before treatment and at the end of the study after 4 weeks of therapy.

P300 potential of healthy controls was recorded one time using the same paradigm and same stimuli parameters.

Parameters of P300 potential of patients and controls were compared before treatment by means of Mann-Whitney nonparametric U-test for unpaired variables. Statistical significance of changes of mean values of P300 parameters during therapy was evaluated using Wilcoxon's test for paired variables. All cases of correlation were analyzed by calculating nonparametric Spearman correlation coefficients. Data were analyzed using Microsoft Office Excel 2003 and STATISTICA 8.0 software.

2.2. Study of effect of electroconvulsive therapy on auditory event-related potential P300.

2.2.1. Subjects

There were 38 patients studied – 21 females and 17 males. Average age was 44.5±13.5 years. Oldest patient was 72 years old, youngest – 22 years old. For data analysis all patients were divided into two groups according to their diagnosis and into two groups according to their age (Table 2.2 and Table 2.3 respectively). First diagnosis group was a group of patients with schizophrenia spectrum disorders (diagnoses, which indexes start with F2) and second group was composed of patients with mood disorders (diagnoses, which indexes start with F3). According to age there was a group of younger patients (age up to 49 years) and a group of older patients (age from 49 years).

Age-matched control groups of healthy subjects were composed for groups of diagnoses and for a common group which comprised all ECT patients.

Exclusion criteria were the same as in pharmacological studies.

Table 2.2. Characteristics of groups of patients according to their diagnoses and groups of matched controls

	SSD	Controls	Mood disorders	Controls
Number of participants	22	22	16	16
Average age	37.9±12.3 years	38.0±12.1 years	53.6±9.1 years	50.5±6.9 years
Males	12	14	5	6
Females	10	8	11	10

Note: SSD – schizophrenia spectrum disorders

Table 2.3. Characteristics of groups of patients according to their age

	Younger patients	Older patients
Number of participants	21	17
Average age	34.5±8.2 years	56.8±6.8 years
Males	11	6
Females	10	11

2.2.2. Study design

Event-related potential P300 was recorded two times - one day before the first ECT procedure and next day after the last.

At first the parameters of P300 potential were analyzed in the common group of patients and after that in separate groups. Clinical symptoms were evaluated by means of PANSS test in the case of schizophrenia spectrum disorders and using Hamilton Depression Rating Scale HAM-D (Hamilton, 1960; Williams, 1988) and Montgomery-Åsberg Depression Rating Scale MADRS (Montgomery and Åsberg, 1979) in the case of mood disorders.

Psychiatric scales were filled by psychiatrists.

Statistical analysis was the same as in pharmacological studies.

2.2.3. ECT procedure

In the Republican Vilnius Psychiatric Hospital modified electroconvulsive therapy is applied – the patient before the procedure receives anesthesia and muscle relaxants for suppression of motor seizures.

ECT is prescribed by psychiatrist. ECT procedures are carried out by experienced anesthesiologist every second day (excluding weekends) in the Department of Resuscitation and Intensive Therapy of RVPH using ECT machine „Thymatron^{TM} DGx“ (Somatics, Inc.). Number of procedures depends on the initial clinical status of the patient and the therapeutic effect. For anesthesia solution of sodium thiopental (2-5 mg/kg) is administered. Muscle relaxation is achieved with suxamethonium chloridum (0,5-1 mg/kg) (Bowley and Walker, 2004). Stimulation electrodes are placed bilaterally (Fig. 2.1.). One EEG channel for measurements of induced bioelectrical seizure parameters is recorded with 2 electrodes placed above left and right eyebrows (Fig. 2.1). Psychiatrist sets the stimulation parameters according to the age of the patient as it was found that maximum energy of stimulation needed to induce generalized seizure in the cortex is related to the age of the subject (Sackeim et al., 1987; Boylan et al., 2000; Benbow, 2005). One of the features of the „Thymatron^{TM} DGx“ is that with the “percent energy” dial the physician sets the electrical charge (i.e. quantity of electrons) to be delivered, which is adjustable in 20 equal increments of 25.2 milliCoulombs (mC). For a 1 ms pulsewidth each increment ads 28 pulses from 28 to 560. At maximum setting (100

percent energy on the stimulus dial) the delivered charge is 504 mC, number of pulses is 560 and stimulus duration is 4 s. For stimulation a brief, pulsed, bidirectional, square wave stimulus (Fig. 2.2) with a current fixed at 0.9 A (regardless of the impedance across the stimulation electrodes) is delivered (Swartz and Abrams, 1994).

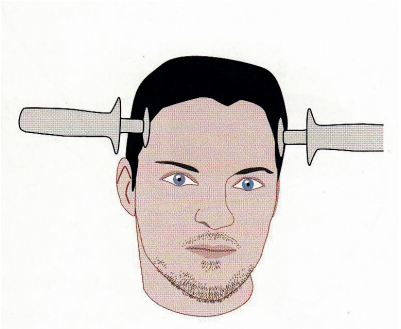

Fig. 2.1. Electrode position for bilateral ECT.

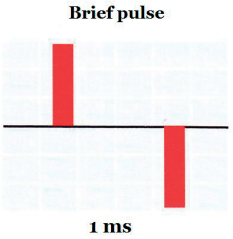

Fig. 2.2. ECT stimulus. „Thymatron^{TM} DGx“ delivers brief pulses of 1 ms duration.

2.2.4. ECT measures.

There were 4 measures of ECT procedures recorded. Apart from the number of ECT procedures and percent energy of delivered stimulus two measures of quality of induced convulsive seizures were also used in the study. These measures are seizure energy index (SEI) and postictal suppression index (PSI). Studies showed that SEI and PSI indices correlate better with therapeutic effect of ECT then duration of seizure (Weiner et al., 1991; Nobler et al., 1993). SEI is obtained when „Thymatron^{TM} DGx“

integrates amplitude of EEG throughout the duration of the seizure and multiplicates mean integrated amplitude (in μV^2) by seizure duration. A seizure energy index below 550 suggests that restimulation be considered at a higher dose. The PSI reflects how quickly and completely the EEG amplitude falls just after the end of the seizure. It is computed as the 3-second mean amplitude beginning 0.5 s after seizure end, divided by mean 3-second peak amplitude obtained during the seizure, and expressed as the percent suppression (range 0-100 percents). A PSI below 74 percents suggests that restimulation be considered at a higher dose.

2.3. Study of the influence of metaglosotherapy on the parameters of P300 potential.

2.3.1. Subjects and study design.

The mean age of 11 men who participated in the program was 47.4±6.4 years (the youngest was 38 years old and the oldest 57); their education was secondary or unfinished secondary; 8 participants were diagnosed with continuous, paranoid schizophrenia; 3 participants with episodic schizophrenia, with progressive deficit according to ICD-10 criteria; the length of treatment at psychiatric institutions ranged from 4 to 27 years (mean duration 17 years); their social adaptation is disturbed, they are not able to live on their own, they live in a nursing home for people with mental disability (they were in hospital because of the disorder exacerbation) or are waiting to live there.

All patients received antipsychotic therapy both before the MGT and during MGT. They also got anticholinergic medication. It was pursued to maintain the dosage and combination of medicaments stable throughout the therapy.

Control group of 11 healthy male subjects was also composed (average age was 47.9±7.3 years – youngest was 36 years, oldest – 60 years).

P300 potential was recorded two times for patients – pre-treatment and after 3 months of therapy, while for the control group – once. In addition to ERP recording psychological assessment of each patient was carried out before the beginning of the program and after it.

Three psychological tests were applied:

- *Schulte tables*: a method for evaluation of speed of sensorimotor reactions, focusing and relocating of attention (Bleicher et al., 2002). The result is recorded as average time of test performance on 5 tables and expressed in seconds.
- *10 words memorizing test*: subject is asked to memorize and to recall 10 two-syllable words. The index of effectiveness of memorizing is obtained – it is ratio between number of recalled words during *n* repetitions and number of repetitions (Bleicher et al., 2002).
- *WAIS (Wechsler Adult Intelligence Scale) Digit Symbol subtest*: test for measurement of psychomotor reactions speed and learning ability (Joy et al., 2000).

Statistical analysis of data was the same as in pharmacological studies and ECT study.

2.3.2. Course of metaglossotherapy

Metaglosotherapy was based on the book "Language…a hope. An introduction to metaglossotherapy" by Dr. A.C. Matulis (Matulis, 1977) where the method of MGT was described. In process of the work the method was adapted and developed further.

MGT was carried out at the Vilnius Republican Psychiatric Hospital, at the department of chronic long-stay patients. The program lasted three months, 3 sessions a week. Duration of the session was 30 - 40 minutes. Sessions were guided by the psychiatrist (man) and the psychologist (women). Two languages were taught: English (6 patients) and esperanto for those who had studied English before (5 patients).

Usual teaching methods would not be sufficient to support patients motivation, so different visual aids (posters, pictures), toys and real things, elements of psychodrama (for instance, performing situations such as "shopping" or "acquaintance in a coffee-bar"), were used. The patients were taught not only of new words and formulation of sentences, but their social skills were developing as well. Lessons were carried out in a form of questions – answers. At first teachers were asking questions and patients had to answer then vice versa.

2.4. P300 recording and analysis.

Auditory P300 potential was elicited applying the same "odd-ball" paradigm and the same parameters of stimuli in all studies. The measurements also were the same. ERPs were recorded using „Galileo Sirius Mizar" (EBNeuro company, Florence, Italy) digital EEG and evoked potentials system. All recordings were made in electrically shielded chamber.

Three active electrodes were placed according to the international "10-20" system at Fz (frontal), Cz (central) and Pz (parietal) sites (Fig. 2.3). Reference electrodes (A1 and A2) were placed on earlobes and linked together. Ground electrode was at Fpz site. Ag/AgCl bridge electrodes were used.

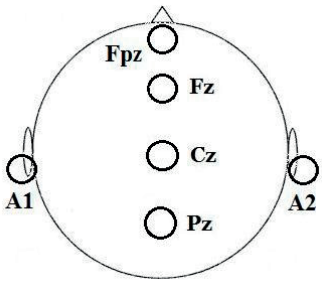

Fig. 2.3. The scheme of electrode placement for recording of auditory P300 potential. Fz, Cz, and Pz – active electrodes; A1 and A2 – reference electrodes; Fpz – ground electrode.

In this work the methodology for eliciting and recording P300 was based on principles standardized and recommended by International and American Societies of Clinical Neurophysiologists for use in neurophysiologic laboratories (Tables 2.4 and 2.5). Guidelines for using event-related potentials in clinical research were also taken into account (Duncan et al., 2009).

Table 2.4. Stimulus factors for eliciting P300 used in RVPH (Korostenskaja et al., 2000)

PARAMETER	COMMENT
Type of stimulus	Tones
Stimulus: deviant (target) stimulus standard stimulus	 2000 Hz 1000 Hz
Interstimulus interval	1500 - 2000 ms
Stimulus probability: deviant (target) stimulus standard stimulus *Deviant/standard stimulus ratio*	 20% 80% 1:4
Stimulus intensity: deviant (target) stimulus standard stimulus	 60 dB both stimuli
Stimulus duration	50 ms

Table 2.5. Electrophysiological recording of P300

PARAMETER	COMMENT
Analysis epoch	1000 ms
Prestimulus baseline	100 ms
Minimum number of artifact-free averages	25
Montage: Active electrodes Ground electrode Reference electrodes	Monopolar lead Fz, Cz, Pz Fpz A1, A2
Artifact rejection	>100μV
Bandpass of amplifiers	0.01 Hz – 30 Hz
Participant and task: Position Eyes Active task	 Seated Open Attention to stimuli required (counting of target stimuli)

Tones were presented through hi-fi earphones for audiography „Telephonics TDH-39P“. Responses to deviant and standard stimuli were averaged separately. Two curves were obtained – one reflecting brain response to frequent stimuli (with standard sensory P1-N1-P2 complex), while the other represents auditory information processing comprising sensory and cognitive (waves N2-P3-N3) complexes.

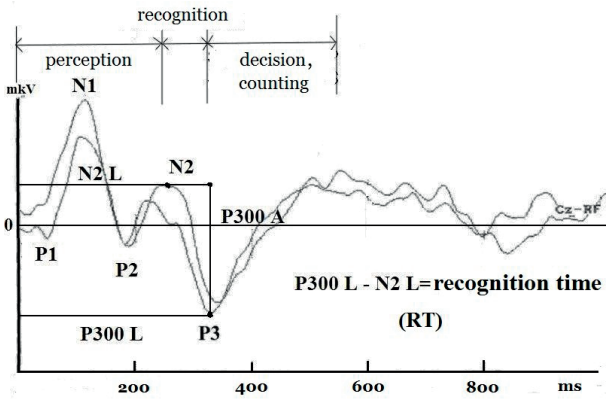

Fig. 2.4. Measurements of P300 cognitive complex: N2L – N2 latency in ms, P300L – P300 latency in ms, P300 A – P300 amplitude in μV, RT – recognition time of target stimulus.

Four parameters of P300 were measured in this work (Fig. 2.4):

1) N2 latency in milliseconds;
2) P300 latency in milliseconds;
3) P300 amplitude (measured "peak-to-peak", i.e. taken difference between amplitudes of N2 and P300 waves measured from the baseline) in microvolts (μV);
4) recognition time of target stimulus (RT) (difference between latencies of N2 and P300) in milliseconds (Polich J. and Kok A., 1995; Korostenskaja et al., 2003).

N2 and P300 waves can be viewed as separate components, however in this work, taking into account that the main aim was to study difference between ERPs of patients and healthy controls and changes under the influence of various therapies while the conditions of eliciting and recording was always the same, all measurements (including differences) are referred as parameters of P300.

3. Results.

3.1. Effect of atypical antipsychotic risperidone on the auditory event-related potential P300.

3.1.1. Effect of risperidone on the parameters of P300 in patients with schizophrenia.

When the measures of P300 of schizophrenia patients (N=15) were compared with measures of healthy controls it was found that latencies of N2 and P300 were statistically significantly prolonged (Table 3.1 and Fig. 3.1). Amplitude of P300 was smaller than in healthy controls, but the difference was insignificant. Mean values of recognition time of target stimulus (RT) were almost equal.

Table 3.1. P300 latencies of healthy controls (P3 L N) and patients with schizophrenia before risperidone therapy (P3 L Before)

Electrode	Parameter	Mean (ms), N=15	SD	p=
Fz	P3 L N	324.5	17.0	
	P3 L Before	358.5	14.4	**0.001**
Cz	P3 L N	329.9	11.4	
	P3 L Before	360.3	22.2	**0.004**
Pz	P3 L N	334.5	11.1	
	P3 L Before	353.5	17.1	**0.008**

Note: L – latency, N – healthy controls, p – significance level of the means difference (p value in bold font represents statistically significant difference between means), label P3 is used instead of P300 for brevity reasons

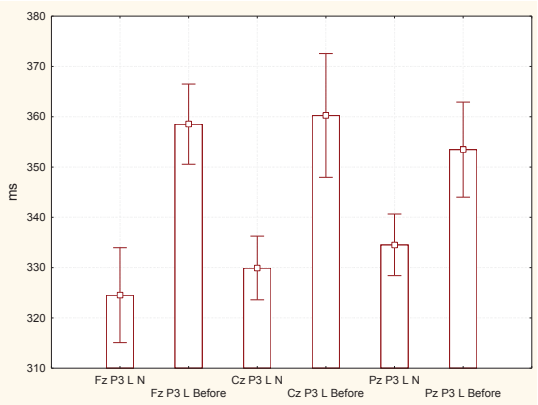

Fig. 3.1. P300 latencies of healthy controls (P3 L N) and patients with schizophrenia before risperidone therapy (P3 L Before) (N=15). Means are presented. Whiskers: mean±0.95 confidence level.

Absolute changes of P300 parameters after 2 and 4 weeks of risperidone therapy were inconsiderable and differences of means were statistically insignificant. The largest change was in RT at Cz electrode – it shortened from 122 ms ±26.3 before therapy to 109.5±33.1 ms after 2 weeks.

3.1.2. Effect of risperidone on the parameters of P300 in patients with schizoaffective disorder.

As in the group of schizophrenia patients the P300 potential was abnormal, but at lesser extent. Latency of N2 was longer, but differences of means were insignificant. P300 latency across all three electrodes was significantly prolonged (Table 3.2, Fig. 3.2) and P300 amplitude was significantly smaller at frontal area (Fz), (Table 3.3, Fig. 3.3).

Table 3.2. P300 latencies of healthy controls (P3 L N) and patients with schizoaffective disorder before risperidone therapy (P3 L Before)

Electrode	Parameter	Mean (ms) N=11	SD	p=
Fz	P3 L N	324.7	19.2	
	P3 L Before	362.7	28.6	**0.013**
Cz	P3 L N	328.0	13.8	
	P3 L Before	356.2	21.0	**0.008**
Pz	P3 L N	332.3	13.3	
	P3 L Before	364.7	24.2	**0.008**

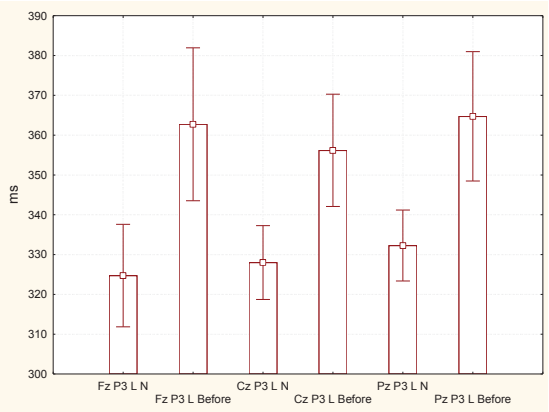

Fig. 3.2. P300 latencies of healthy controls (P3 L N) and patients with schizoaffective disorder before risperidone therapy (P3 L Before) (N=11).

Table 3.3. P300 amplitudes of healthy controls (P3 A N) and patients with schizoaffective disorder before risperidone therapy (P3 A Before)

Electrode	Parameter	Mean (μV) N=11	SD	p=
Fz	P3 A N	20.0	5.1	
	P3 A Before	14.9	6.3	**0.033**
Cz	P3 A N	18.6	6.0	
	P3 A Before	15.0	6.4	0.182
Pz	P3 A N	17.4	4.4	
	P3 A Before	15.3	6.1	0.424

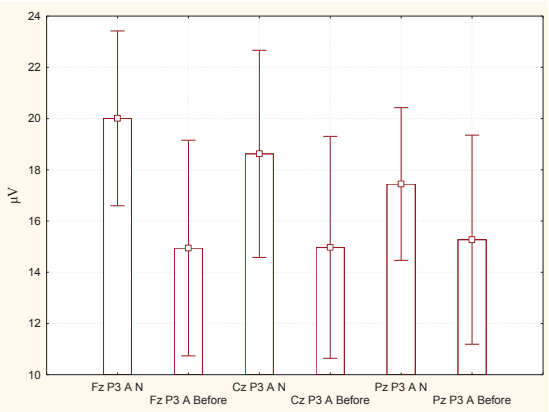

Fig. 3.3. P300 amplitudes of healthy controls (P3 A N) and patients with schizoaffective disorder before risperidone therapy (P3 A Before) (N=11).

Effect of risperidone on P300 parameters after 2 and 4 weeks of therapy in the group of schizoaffective disorder was slightly more marked than in schizophrenia group. However statistically significant differences of means were found only after two weeks of therapy – mean latency of N2 has shortened at Fz from 239.3±15.8 ms at baseline to 233.8±13.2 ms after 2 weeks, (p=0.037), latency of P300 also have shortened only at one area – Cz – from 356.2±21 ms iki 339.5±18.3 ms (p=0,018). P300 amplitude slightly but insignificantly increased. Mean RT duration has shortened significantly also only at Cz – from 118.0±21.6 to 105.8±24.4 ms (p=0.012). However after 4 weeks of therapy there were no more statistically significant differences of P300.

3.1.3. Effect of risperidone on clinical symptoms and correlation of P300 parameters with PANSS scores.

There was considerable and significant improvement in clinical symptoms after 4 weeks of therapy with risperidone. Significantly decreased not only mean overall score, but also mean scores of all three subtests (positive symptoms, negative symptoms and general psychopathology) (Table 3.4).

Table 3.4. PANSS scores at baseline and after 4 weeks of risperidone therapy.

Test	Mean score, N=14	SD	p<
Positive symptoms before	20.7	5.3	
Positive symptoms after	12.3	3.6	**0.001**
Negative symptoms before	21.9	5.0	
Negative symptoms after	17.4	4.3	**0.002**
General psychopathology before	51.5	8.9	
General psychopathology after	31.6	6.9	**0.001**
PANSS before	94.1	16.2	
PANSS after	62.8	12.1	**0.001**

Analysis of correlation between measures of P300 and PANSS scores before therapy has showed that abnormal P300 amplitude at Fz ($r=-0.64$, $p<0.05$) and Pz ($r=-0.70$, $p<0.05$) significantly negatively correlated with negative symptoms of schizophrenia – the smaller was the amplitude the more severe negative symptoms were. The latency of P300 at Fz correlated positively and significantly ($r= 0.57$, $p<0.05$) with the score of positive symptoms. All other coefficients of correlation (45 out of 48) were statistically not significant.

Correlation between changes of P300 measures and PANSS scores under the influence of risperidone was strongest and statistically significant between the amplitude of P300 at electrode Pz and negative symptoms ($r=-0.56$, $p<0.05$), general psychopathology ($r=-0.56$, $p<0.05$) and overall score of PANNS ($r=-0.55$, $p<0.05$). The correlation was negative – the more increased the amplitude, the larger improvement of symptoms was recorded. The latency of P300 also correlated negatively with changes of scores of general psychopathology ($r=-0.58$, $p<0.05$) and overall score of PANSS ($r=-0.55$, $p<0.05$).

3.2. Effect of quetiapine on the parameters of P300 in patients with schizoaffective disorder.

3.2.1. Parameters of P300 potential before quetiapine treatment.

Three parameters of P300 out of four in the group of patients (N=10) have differed significantly as compared to healthy controls (N=10) – patients had longer latencies of N2 and P300 across all three electrodes (Tables 3.5, Fig. 3.4), while the

amplitude of P300 was significantly smaller at Cz and Pz (Table 3.6, Fig. 3.5). Duration of RT was also longer but difference of means was insignificant.

Table 3.5. P300 latencies of healthy controls (P3 L N) and patients with schizoaffective disorder before quetiapine therapy (P3 L Before).

Parameter	Mean (ms) N=10	SD	p=
Fz P3 L N	325.1	23.1	
Fz P3 L Before	396.2	65.1	**0.013**
Cz P3 L N	333.5	21.2	
Cz P3 L Before	397.7	61.3	**0.008**
Pz P3 L N	337.8	22.1	
Pz P3 L Before	398.3	59.4	**0.005**

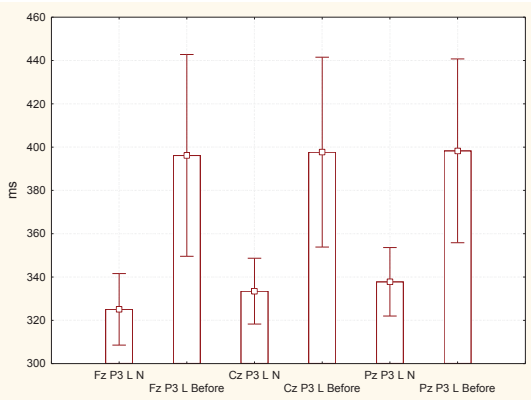

Fig. 3.4. P300 latencies of healthy controls (P3 L N) and patients with schizoaffective disorder before quetiapine therapy (P3 L Before) (N=10).

Table 3.6. P300 amplitudes of healthy controls (P3 A N) and patients with schizoaffective disorder before quetiapine therapy (P3 A Before)

Parameter	Mean (μV) N=10	SD	p=
Fz P3 A N	15.1	4.9	
Fz P3 A Before	11.9	5.6	0.169
Cz P3 A N	17.6	5.1	
Cz P3 A Before	10.5	3.0	**0.022**
Pz P3 A N	16.1	4.3	
Pz P3 A Before	8.7	1.8	**0.011**

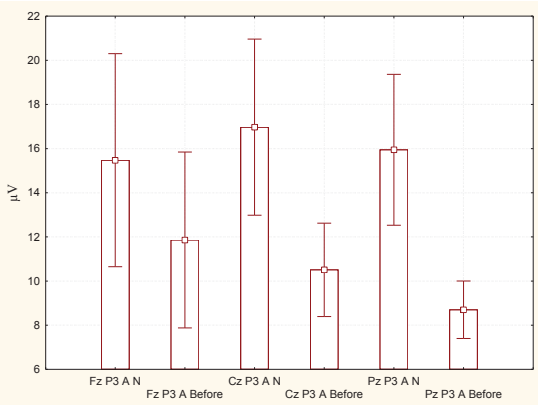

Fig. 3.5. P300 amplitudes of healthy controls (P3 A N) and patients with schizoaffective disorder before quetiapine therapy (P3 A Before) (N=10).

There were no statistically significant coefficients of correlation between P300 parameters at baseline and severity of clinical symptoms as measured with PANSS before quetiapine therapy.

3.2.2. Effect of quetiapine therapy on parameters of P300 potential.

Clinical symptoms of schizophrenia have improved considerably and significantly after 4 weeks of quetiapine therapy. Significantly has decreased not only overall score of PANSS, but also scores of all three subtests (Table 3.7).

Table 3.7. PANSS scores at baseline and after 4 weeks of quetiapine therapy

Test	Mean score (N=10)	SD	p=
Positive symptoms before	18.3	5.4	
Positive symptoms after	10.8	2.1	**0.01**
Negative symptoms before	19.2	5.7	
Negative symptoms after	16.0	4.4	**0.02**
General psychopathology before	53.5	8.2	
General psychopathology after	33.0	4.2	**0.01**
PANSS before	91.0	14.4	
PANSS after	59.2	8.6	**0.01**

When P300 parameters of patients with schizoaffective disorder at baseline were compared with P300 measures it was found that already after 2 weeks of quetiapine

therapy there was significant shortening of P300 latency at all three areas of interest. Improvement in latency even became more marked after 4 weeks of therapy (Table 3.8, Fig. 3.6). In addition, after 4 weeks significant changes are recorded in duration of recognition time of target stimulus (Table 3.9, Fig. 3.7).

Table 3.8. P300 latencies at baseline (P3 L Before), after 2 (P3 L 2) and 4 weeks (P3 L 4) of quetiapine therapy

Parameter	Mean (ms), N=10	SD	p=
Fz P3 L Before	396.2	65.1	
Fz P3 L 2	364.4	61.7	**0.037**
Fz P3 L 4	339.7	37.5	**0.022**
Cz P3 L Before	397.7	61.3	
Cz P3 L 2	364.7	61.5	**0.028**
Cz P3 L 4	335.5	38.0	**0.007**
Pz P3 L Before	398.3	59.4	
Pz P3 L 2	363.4	62.5	**0.017**
Pz P3 L 4	337.1	33.6	**0.005**

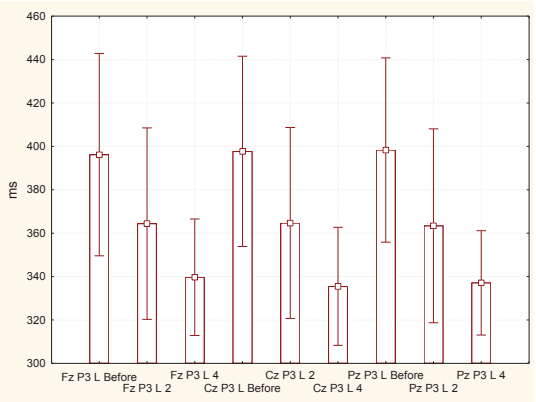

Fig. 3.6. P300 latencies at baseline (P3 L Before), after 2 (P3 L 2) and 4 weeks (P3 L 4) of quetiapine therapy (N=10).

Table 3.9. Recognition time of target stimulus at baseline (RT Before), after 2 (RT 2) and 4 weeks (RT 4) of quetiapine therapy

Parameter	Mean (ms), N=10	SD	p=
Fz RT Before	133.0	27.0	
Fz RT 2	116.2	27.4	0.074
Fz RT 4	86.3	33.0	**0.028**
Cz RT Before	134.3	27.6	
Cz RT 2	117.8	32.4	0.074
Cz RT 4	86.5	30.1	**0.013**
Pz RT Before	128.7	25.4	
Pz RT 2	112.4	34.8	0.059
Pz RT 4	89.4	33.1	**0.011**

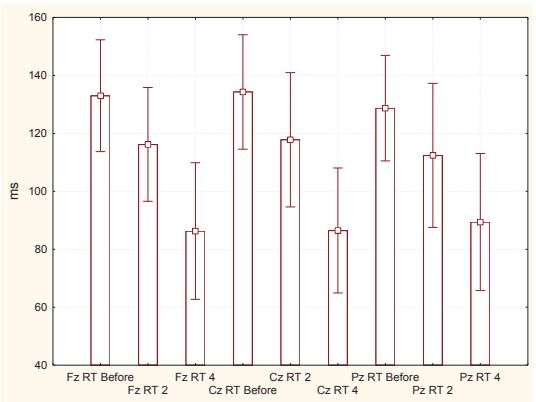

Fig. 3.7. Recognition time of target stimulus at baseline (RT Before), after 2 (RT 2) and 4 weeks (RT 4) of quetiapine therapy (N=10).

Analysis of correlation between changes of P300 measures and scores of PANSS under the influence of quetiapine therapy has revealed several significant relations. Significant positive correlation was noticed between changes in P300 latency at Fz ($r= 0.68$, $p<0.05$) and Pz ($r= 0.65$, $p<0.05$) and changes of negative symptoms. At Cz coefficient of correlation was close to statistically significant ($r= 0.627$). Correlation between changes in P300 amplitude at Cz and Pz ($r= -0.76$ and $r= - 0.83$ respectively, $p<0.05$) and changes in positive symptoms was significantly negative. It was also significant and negative between P300 amplitude at Pz and overall PANSS score ($r=0.634$, $p<0.05$). One more significant coefficient of correlation was found – negative

correlation between changes in RT duration and changes in positive symptoms. All other coefficients of correlation (42 out of 48) were not significant.

3.3. Effect of ECT on auditory event-related potential P300

3.3.1. Effect of ECT on auditory event-related potential P300 in schizophrenia spectrum disorders.

When parameters of P300 potential of the patients with schizophrenia spectrum disorders (N=22), who were treatment-resistant and were referred to receive the course of ECT, were compared at baseline with measures of P300 of healthy controls (N=22), it was found that auditory event-related potential P300 has differed significantly in three parameters out of four (only comparison of P300 latencies and P300 amplitudes is shown in Tables 3.10, 3.11 and Fig. 3.8, 3.9).

Table 3.10. P300 latencies of healthy controls (P3 L N) and patients with schizophrenia spectrum disorders before ECT (P3 L Before)

Parameter	Mean (ms), N=22	SD	p=
Fz P3 L N	324.4	21.4	
Fz P3 L Before	360.9	43.2	**0.002**
Cz P3 L N	331.9	17.3	
Cz P3 L Before	361.5	42.7	**0.009**
Pz P3 L N	337.6	20.2	
Pz P3 L Before	363.1	41.9	**0.026**

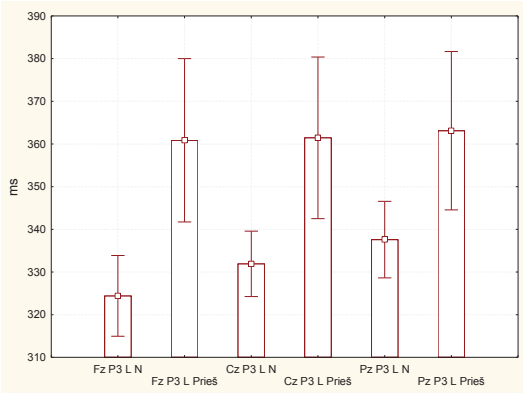

Fig. 3.8. P300 latencies of healthy controls (P3 L N) and patients with schizophrenia spectrum disorders before ECT (P3 L Before) (N=22).

Table 3.11. P300 amplitudes of healthy controls (P3 A N) and patients with schizophrenia spectrum disorders before ECT (P3 A Before)

Parameter	Mean (μV), N=22	SD	p=
Fz P3 A N	16.1	5.8	
Fz P3 A Before	10.8	6.1	**0.013**
Cz P3 A N	16.1	5.4	
Cz P3 A Before	10.3	5.0	**0.008**
Pz P3 A N	14.8	5.0	
Pz P3 A Before	10.4	5.6	**0.010**

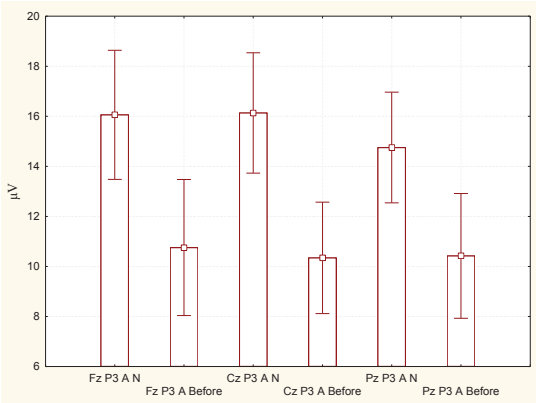

Fig. 3.9. P300 amplitudes of healthy controls (P3 A N) and patients with schizophrenia spectrum disorders before ECT (P3 A Before) (N=22).

Mean recognition time of target stimulus of patients was close to that measured in the group of healthy controls.

Comparison of P300 parameters at baseline with measures after the course of ECT in the group of patients with schizophrenia spectrum disorders (group F2x) has revealed that all temporal measurements (latencies of N2, P300 and duration of RT) have shortened, but changes were not significant. Only the increase in the amplitude was statistically significant across all three areas (Table 3.12, Fig. 3.10).

Table 3.12. P300 amplitudes of patients with schizophrenia spectrum disorders at baseline (P3 A Before) and after ECT (P3 A After)

Parameter	Mean (μV), N=22	SD	p=
Fz P3 A Before	10.8	6.1	
Fz P3 A After	13.6	7.4	**0.050**
Cz P3 A Before	10.3	5.0	
Cz P3 A After	13.0	6.1	**0.033**
Pz P3 A Before	10.4	5.6	
Pz P3 A After	12.9	5.7	**0.048**

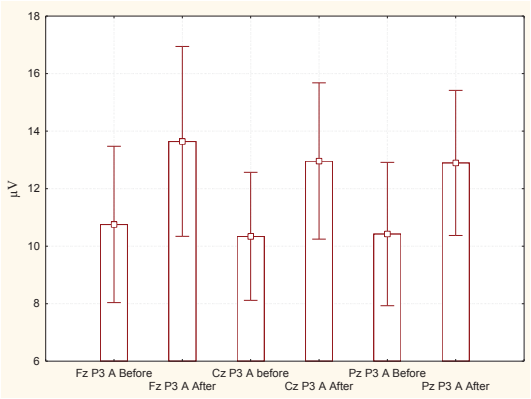

Fig. 3.10. P300 amplitudes of patients with schizophrenia spectrum disorders at baseline (P3 A Before) and after ECT (P3 A After) (N=22).

3.3.2. Effect of ECT on auditory event-related potential P300 in mood disorders.

When P300 measures of patients with mood disorders (group F3x) at baseline were compared with data of subjects from the control group statistically significant differences were found in mean values of latency of N2 at all three electrodes (Table 3.13 and Fig. 3.11) and latency of P300 at Fz (Table 3.14 and Fig. 3.12). Latencies were prolonged and amplitude was smaller.

Table 3.13. N2 latencies of healthy controls (N2 L N) and patients with mood disorders before ECT (N2 L Before)

Parameter	Mean (ms), N=16	SD	p=
Fz N2 L N	215.7	31.0	
Fz N2 L Before	242.0	29.9	**0.024**
Cz N2 L N	210.6	29.7	
Cz N2 L Before	239.5	29.6	**0.023**
Pz N2 L N	209.0	23.1	
Pz N2 L Before	239.3	27.7	**0.015**

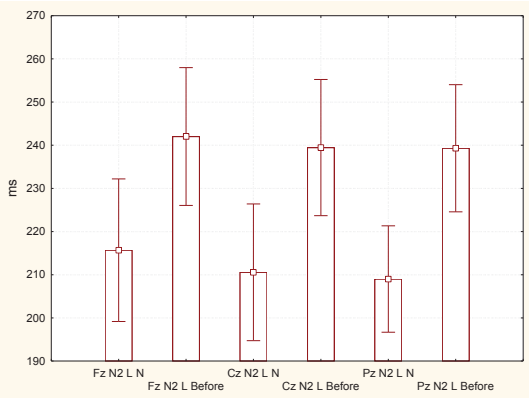

Fig. 3.11. N2 latencies of healthy controls (N2 L N) and patients with mood disorders before ECT (N2 L Before) (N=16).

Table 3.14. P300 latencies of healthy controls (P3 L N) and patients with mood disorders before ECT (P3 L Before)

Parameter	Mean (ms), N=16	SD	p=
Fz P3 L N	324.4	20.1	
Fz P3 L Before	361.6	41.5	**0.008**
Cz P3 L N	330.0	16.3	
Cz P3 L Before	354.7	46.2	0.070
Pz P3 L N	339.3	19.4	
Pz P3 L Before	355.5	45.4	0.233

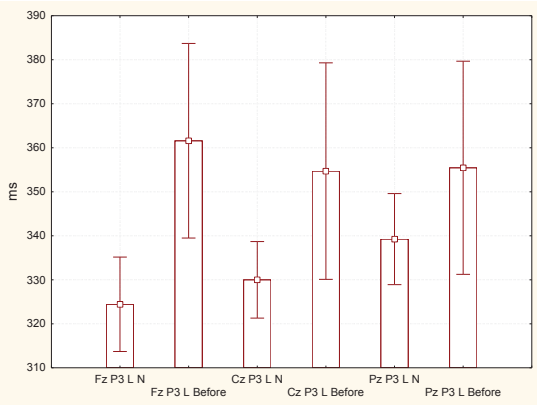

Fig. 3.12. P300 latencies of healthy controls (P3 L N) and patients with mood disorders before ECT (P3 L Before) (N=16).

The results of influence of ECT on P300 in this group have slightly differed from those received in schizophrenia spectrum disorders group. The overall tendency of the changes in P300 measures remained the same, but statistical significance was different – considerable change was established only in P300 amplitude at the central area (Cz) (Table 3.15, Fig. 3.13).

Table 3.15. P300 amplitudes of patients with mood disorders at baseline (P3 A Before) and after ECT (P3 A After)

Parameter	Mean (μV), N=16	SD	p=
Fz P3 A Before	12.7	6.1	
Fz P3 A After	14.5	4.1	0.163
Cz P3 A Before	11.9	5.2	
Cz P3 A After	15.1	4.4	**0.039**
Pz P3 A Before	12.3	4.1	
Pz P3 A After	14.5	5.1	0.070

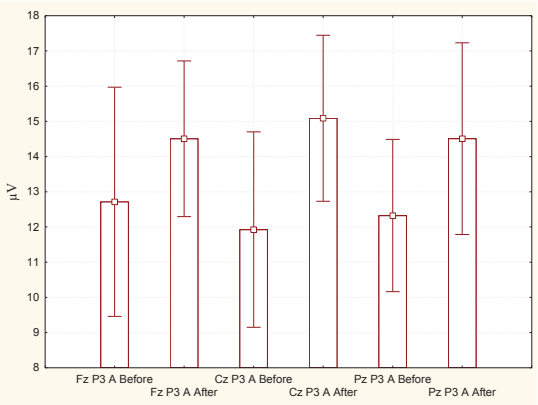

Fig. 3.13. P300 amplitudes of patients with mood disorders at baseline (P3 A Before) and after ECT (P3 A After) (N=16).

3.3.3. Influence of ECT on the clinical symptoms and their correlation with P300 parameters.

Because clinical symptoms were evaluated using different clinical scales for patients with different diagnoses, the correlation between P300 parameters and scores of particular test was analyzed for all tested patients from both groups.

Clinical symptoms of patients with schizophrenia spectrum disorders were measured using PANSS test. There was considerable and statistically significant improvement in mean scores of all subscales and overall value of PANSS after the course of ECT (Table 3.16, Fig. 3.14).

Table 3.16. PANSS scores at baseline and after ECT

Symptoms	Mean score, (N=21)	SD	p=
Positive symptoms before	24.3	9.4	
Positive symptoms after	13.3	7.0	**0.0001**
Negative symptoms before	28.3	7.1	
Negative symptoms after	17.6	4.0	**0.0001**
GPP before	64.8	11.9	
GPP after	33.2	10.7	**0.0001**
PANSS before	117.4	25.1	
PANSS after	64.0	19.3	**0.0001**

Note: GPP – general psychopathology

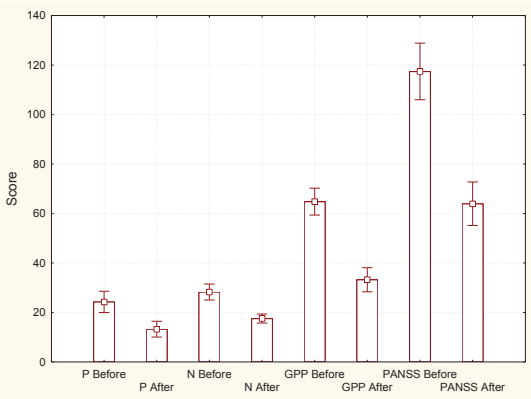

Fig. 3.14. PANSS scores at baseline and after ECT (N=21). P – positive symptoms, N – negative symptoms, GPP - general psychopathology.

In the case of mood disorders there were two tests used – Hamilton Depression Rating Scale (HAMD) (Table 3.17, Fig. 3.15) and Montgomery-Åsberg Depression Rating Scale (MADRS) (Table 3.18, Fig. 3.15). The mean scores of both depression rating scales diminished markedly and statistically significantly. It must be noted, that in the case of schizoaffective disorder in the group with schizophrenia spectrum disorders one of the depression rating scales could have been applied.

Table 3.17. Scores of Hamilton Depression Rating Scale (HAMD) at baseline and after ECT

Scale	Mean score, N=19	SD	p=
HAMD Before	31.3	7.9	
HAMD After	6.8	6.4	**0.0001**

Table 3.18. Scores of Montgomery-Åsberg Depression Rating Scale (MADRS) at baseline and after ECT

Scale	Mean score, N=9	SD	p=
MADRS Before	37.9	7.4	
MADRS After	10.1	4.6	**0.008**

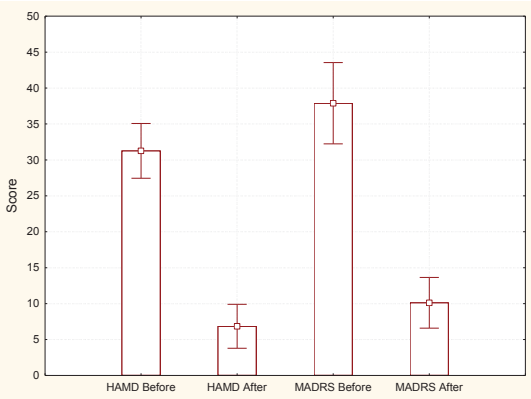

Fig. 3.15. Scores of Hamilton Depression Rating Scale (HAMD, N=19) and Montgomery-Åsberg Depression Rating Scale (MADRS, N=9) at baseline and after ECT.

Correlation between P300 parameters of the patients with schizophrenia spectrum disorders and scores of PANSS at baseline was significant only for P300 latency at frontal area (Fz, $r=0.49$, $p<0.05$) and parietal area (Pz, $r=0.46$, $p<0.05$).

There was no significant correlation between measures of P300 and HAMD scale scores. MADRS scores significantly negatively correlated only with P300 amplitude at parietal area (Pz, $r=-0.75$, $p<0.05$)

It was attempted to analyze correlation between ECT induced changes of P300 and changes in severity of clinical symptoms of schizophrenia and depression, but there were no statistically significant coefficients of correlation found.

3.3.4. Correlation between P300 parameters and indices of ECT procedure

In order to establish the value of indices of ECT in relation to changes of cognitive functions in the course of ECT the correlation between their mean values (Table 3.19) and changes of P300 parameters was studied (Table 3.20).

Table 3.19. Mean values of ECT procedure indices (N=38)

	Number of procedures	Energy %	SEI	PSI %
Mean value	8.9	32.0	1005.8	84.9
SD	3.1	12.2	278.3	10.5

Note: SEI – seizure energy index, PSI – postictal suppression index

Table 3.20. Coefficients of correlation between indices of ECT procedure and changes of recognition time of target stimulus (RT) after ECT

P300 parameter	Number of procedures	Stimulus energy (%)	SEI	PSI %
Fz RT	**0.33**	**-0.33**	**0.43**	-0.09
Cz RT	**0.33**	-0.29	**0.49**	-0.12
Pz RT	0.23	-0.20	**0.42**	-0.18

Note: SEI – seizure energy index, PSI – postictal suppression index, numbers in bold font indicate statistically significant coefficients of correlation ($p<0.05$)

It was found that most significant positive correlation was between SEI, number of procedures and changes of recognition time of target stimulus (RT). Changes of RT duration at Fz also correlated significantly negatively with mean energy of delivered stimulus. Aftersitive correlation of RT changes with SEI means, that the greater energy of induced bioelectrical seizure, the larger changes of RT. There was significant positive correlation between changes of P300 latency at Fz and number of ECT procedures.

3.3.5. Effect of ECT on the P300 parameters in relation to the age of patients.

It is known that excitability of the brain cortex depends on the age of the subject and with age its level decreases. So the patients of ECT group were divided regardless their diagnosis into two age groups: younger patients (up to 48 years, N=21) and older patients (from 49 years, N=17).

Comparison of P300 parameters of patients from both groups revealed that older patients differed significantly from younger in P300 latency and RT across all electrodes. P300 latency was 339.4±30.8 ms in younger patients vs. 382.3±46.4 ms in older patients at Cz ($p<0.02$), while RT was 101.8±40.5 ms and 132.5±38.9 ms respectively ($p<0.024$). There were no significant differences between mean N2 latency and mean P300 amplitude in younger and older patients.

The effect of ECT on parameters of P300 potential also was different in groups composed according to age. In the group of younger patients N2 latency has shortened, while in the group of older patients N2 latency remained unchanged (249.8 ms at baseline vs. 249.6 ms after ECT at Cz area). P300 latency has shortened slightly in both groups, while amplitude increased, but the increment in P300 amplitude was statistically significant only in the group of older patients (Table 3.21, Fig. 3.16).

Table 3.21. P300 amplitudes of older patients before (P3 A Before) and after ECT (P3 A After)

P300 parameter	Mean, (μV) (N=17)	SD	p=
Fz P3 A Before	12.0	6.3	
Fz P3 A After	15.2	6.2	**0.031**
Cz P3 A Before	11.9	5.2	
Cz P3 A After	15.2	5.6	**0.015**
Pz P3 A Before	12.0	5.0	
Pz P3 A After	15.0	6.2	**0.025**

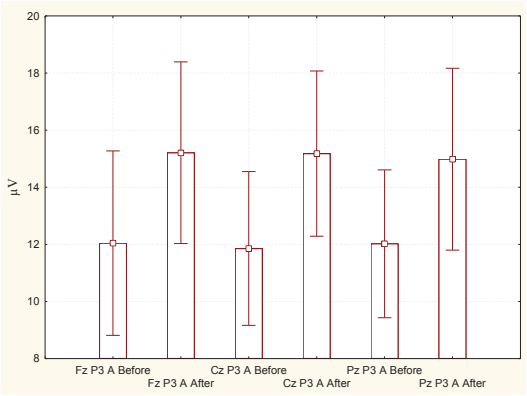

Fig. 3.16. P300 amplitudes of older patients before (P3 A Before) and after ECT (P3 A After) (N=17).

Recognition time of target stimulus in younger patients practically did not changed and in the group of older patients it tended to shorten, but differences were insignificant.

There were differences in correlation between ECT indices and changes of P300 parameters related to age of patients. It is worth to mention that in both groups significant correlation almost exclusively was associated with RT parameter of P300, but in younger patients RT changes at all three electrodes correlated more closely and negatively with mean energy of stimulus (Table 3.22), while in older patients – positively with seizure energy index (Table 3.23).

Table 3.22. Coefficients of correlation between changes in RT and changes in PANSS scores under the influence of ECT in younger patients (N=21)

P300 parameter	Number of procedures	Stimulus energy %	SEI	PSI %
Fz RT	0.33	**-0.50**	0.31	-0.12
Cz RT	0.36	**-0.46**	**0.47**	-0.13
Pz RT	0.29	**-0.46**	0.37	-0.20

Note: SEI – seizure energy index, PSI – postictal suppression index

Table 3.23. Coefficients of correlation between changes in RT and changes in PANSS scores under the influence of ECT in older patients (N=17)

P300 parameter	Number of procedures	Stimulus energy %	SEI	PSI %
Fz RT	0.32	-0.25	**0.62**	0.01
Cz RT	0.30	-0.19	**0.62**	-0.04
Pz RT	0.20	0.00	**0.62**	-0.14

Note: SEI – seizure energy index, PSI – postictal suppression index

3.4. Effect of metaglosotherapy on parameters of P300 potential

3.4.1. Parameters of P300 of patients with schizophrenia before MGT.

Comparison of P300 parameters of patients from the group of MGT (N=11) with measures of healthy controls (N=11) showed that mean latencies of N2 and P300 (only comparison of P300 latencies is shown in Table 3.24 and Fig. 3.17) were significantly prolonged, while mean amplitude of P300 was significantly smaller (Table 3.25 and Fig. 3.18). RT was longer in patients but the difference was insignificant.

Table 3.24. P300 latencies of healthy controls (P3 L N) and patients before MGT (P3 L Before)

Parameter	Mean (ms), N=11	SD	p=
Fz P3 L N	328.5	15.1	
Fz P3 L Before	378.9	35.4	**0.008**
Cz P3 L N	331.0	13.6	
Cz P3 L Before	379.5	34.8	**0.013**
Pz P3 L N	337.1	18.7	
Pz P3 L Before	380.5	33.9	**0.016**

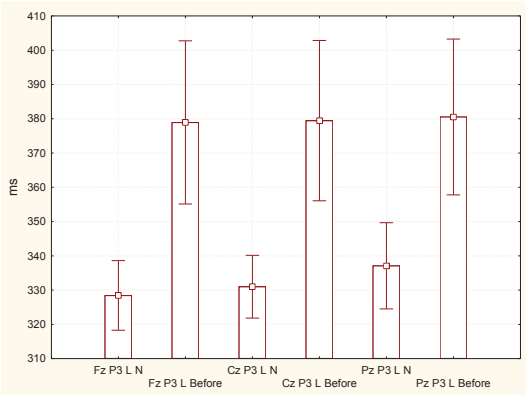

Fig. 3.17. P300 latencies of healthy controls (P3 L N) and patients before MGT (P3 L Before) (N=11).

Table 3.25. P300 amplitudes of healthy controls (P3 A N) and patients before MGT (P3 A Before)

Parameter	Mean (μV), N=11	SD	p=
Fz P3 A N	13.6	5.6	
Fz P3 A Before	4.3	3.6	**0.003**
Cz P3 A N	13.1	5.5	
Cz P3 A Before	4.7	3.5	**0.008**
Pz P3 A N	11.3	4.7	
Pz P3 A Before	4.7	3.4	**0.008**

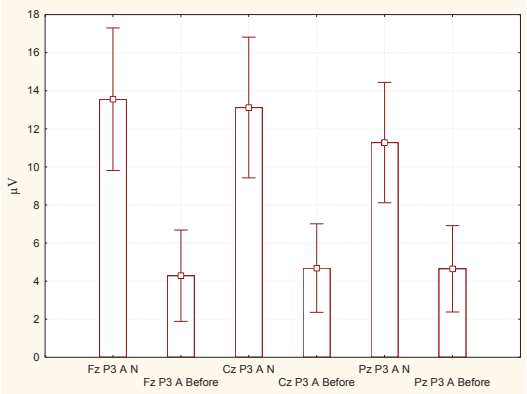

Fig. 3.18. P300 amplitudes of healthy controls (P3 A N) and patients before MGT (P3 A Before) (N=11).

3.4.2. Changes of P300 parameters after MGT.

After the MGT latency of N2 slightly, but not significantly, increased (252±14.8 ms before MGT vs. 265.0±22.5 ms after MGT at Cz, p=0.15). P300 amplitude also increased (4.69±3.46 μV before MGT vs. 7.15±6.83 μV after MGT at Cz, p=0.53) and also insignificantly. However mean P300 latency (Table 3.26, Fig. 3.19) and mean RT (Table 3.27, Fig. 3.20) under the influence of MGT shortened statistically significantly.

Table 3.26. P300 latencies of MGT patients at baseline (P3 L Before) and after MGT (P3 L After)

Parameter	Mean (ms), N=11	SD	p=
Fz P3 L Before	378.9	35.4	
Fz P3 L After	348.3	23.0	**0.041**
Cz P3 L Before	379.5	34.8	
Cz P3 L After	347.6	22.0	**0.041**
Pz P3 L Before	380.5	33.9	
Pz P3 L After	348.7	23.1	**0.033**

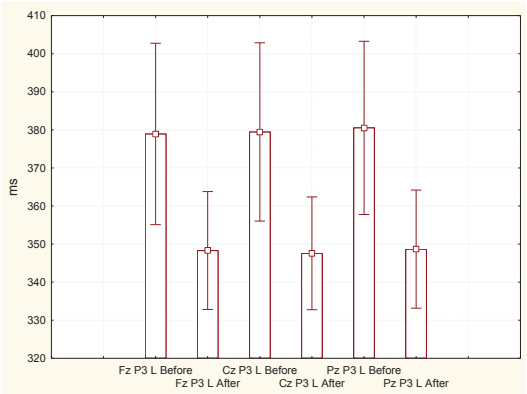

Fig. 3.19. P300 latencies of MGT patients at baseline (P3 L Before) and after MGT (P3 L After) (N=11).

Table 3.27. Recognition time of target stimulus (RT) of MGT patients at baseline (P3 RT Before) and after MGT (P3 RT After)

Parameter	Mean (ms), N=11	SD	p=
Fz RT Before	123.3	35.1	
Fz RT After	82.4	35.3	**0.016**
Cz RT Before	127.6	31.3	
Cz RT After	82.6	34.0	**0.001**
Pz RT Before	128.5	31.3	
Pz RT After	82.8	34.2	**0.013**

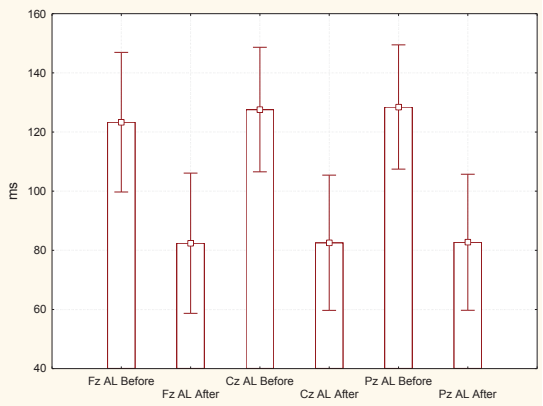

Fig. 3.20. Recognition time of target stimulus (RT) of MGT patients at baseline (RT Before) and after MGT (RT After) (N=11).

Patients of MGT therapy group were tested with three psychological cognitive tests at baseline and after 3 months of MGT. Results of 10 words memorizing test showed significant improvement in memorizing of words after MGT (Table 3.28). Mean time of accomplishing the test of Schulte tables shortened significantly (Table 3.29). Data of mean score of WAIS Digital Symbol test showed improvement after course of MGT (21.5±9.0 score before MGT vs. 24.0±8.9 score after MGT), but the change was insignificant ($p>0.069$).

Table 3.28. Scores of three cognitive tests at baseline and after MGT

Cognitive test	Mean score, (N=11)	SD	p=
10WM Before MGT	5.5	1.5	
10WM After MGT	6.2	1.7	**0.014**
SchT Before MGT	89.0	35.9	
SchT After MGT	76.0	24.2	**0.021**
DS Before MGT	21.5	9.0	
DS After MGT	24.0	8.9	0.069

Note: 10WM – 10 words memorizing test, SchT – Schulte tables, DS – WAIS Digit Symbol

Analysis of correlation between P300 measures and scores of cognitive tests at baseline revealed that significant negative correlation was between P300 latency, duration of RT and scores of 10 words memorizing test (Table 3.43). Coefficients of correlation were significant at all three sites. Significant positive correlation between amplitude of P300 at Cz and score of Schulte test.

Table 3.29. Correlation between P300 measures and scores of cognitive tests at baseline

Parameter	10WM	SchT	DS
Fz N2 L Before	0.00	-0.28	0.35
Cz N2 L Before	-0.10	-0.45	0.50
Pz N2 L Before	-0.10	-0.45	0.50
Fz P3 L Before	**-0.75**	0.08	-0.13
Cz P3 L Before	**-0.75**	0.08	-0.13
Pz P3 L Before	**-0.77**	0.15	-0.21
Fz P3 A Before	-0.10	0.25	0.05
Cz P3 A Before	-0.46	**0.61**	-0.53
Pz P3 A Before	-0.32	0.43	-0.50
Fz RT Before	**-0.72**	0.13	-0.19
Cz RT Before	**-0.74**	0.24	-0.30
Pz RT Before	**-0.77**	0.31	-0.39

Note: 10WM – 10 words memorizing test, SchT – Schulte tables, DS – WAIS Digit Symbol test

Correlation between changes of parameters of P300 and scores of cognitive tests under the influence of MGT was also studied. It was found that changes in P300 latency amplitude correlated negatively and significantly with changes in WAIS Digital Symbol tests scores, while changes in P300 amplitude correlated positively with changes in scores of the same test. Coefficients of correlation were statistically significant across all electrodes (Table 3.30).

Table 3.30 Coefficients of correlation between changes in P300 parameters and changes in cognitive tests scores under the influence of MGT

Parameter	Electrode	10WM	SchT	DS
N2 Latency	Fz	0.55	0.23	-0.54
	Cz	0.52	-0.08	-0.54
	Pz	0.52	-0.08	-0.54
P3 Latency	Fz	0.18	-0.23	**-0.78**
	Cz	0.23	-0.25	**-0.71**
	Pz	0.21	-0.13	**-0.82**
P3 Amplitude	Fz	-0.34	-0.24	**0.79**
	Cz	-0.30	-0.04	**0.82**
	Pz	-0.47	-0.19	**0.81**
RT	Fz	-0.21	-0.25	**-0.63**
	Cz	-0.17	-0.23	-0.51
	Pz	-0.17	-0.19	-0.53

Note: 10WM – 10 words memorizing test, SchT – Schulte tables, DS – WAIS Digit Symbol

3.5. Results of analysis of correlation between scores of PANSS and measures of P300

In order to evaluate possible relationship between clinical symptoms of schizophrenia and P300 parameters at baseline, the correlation between PANSS scores and parameters of P300 of all patients from all groups who underwent testing (14 patients from risperidone group, 10 patients from quetiapine group and 21 patient from ECT group – total number of patients N=45) was analyzed. Only one coefficient of correlation out of 48 was statistically significant, but relatively low – negatively correlated RT at Cz with positive symptoms (r=-0.30).

4. DISCUSSION.

4.1. Influence of atypical antipsychotics on the parameters of auditory P300 potential in schizophrenia spectrum disorders.

Data received in the common group of patients (N=26) before risperidone treatment and compared with data of healthy controls have shown abnormal parameters of P300potential. The most marked difference was in P300 latency – it was significantly prolonged than in healthy controls ($p<0.001$ for all three sites of recording). N2 latency was also significantly prolonged while amplitude of P300 was diminished, but only at Fz the difference was significant. Recognition time of target stimulus was longer in the group of patients, but impairment was insignificant.

There were statistically significant improvements for the PANSS scores after 4 weeks of risperidone treatment. This indicates good antipsychotic action of risperidone. It must be noted that only for one patient PANSS scores have changed a little – his overall PANSS score diminished only by 6 points. So the patients of risperidone group may be viewed as patients who respond to pharmacological treatment. However when the changes of parameters of P300 were evaluated, it was found that effect of risperidone on the event-related potential was insignificant. The only statistically significant change was shortening of P300 latency at Cz after 2 weeks of therapy. After 4 weeks of therapy no statistically significant changes were observed. The absolute changes of the mean values of parameters were also small – latency of P300 has shortened only about 10 ms and amplitude increased– 2-3 μV.

The study of correlation between P300 parameters and scores of clinical symptoms before therapy showed that amplitude of P300 correlated negatively with negative symptoms of schizophrenia, i.e. the more pronounced were the negative symptoms, the more decreased was the amplitude. At the same time, latency of P300 at the frontal area positively correlated with positive symptoms.

When correlation between changes of P300 parameters and PANSS scores under the influence of risperidone was calculated it was noticed that strongest relation was between the amplitude of P300 at parietal area (electrode Pz) and negative symptoms, general psychopathology and overall score of PANNS. The correlation was negative – the more increased the amplitude, the larger improvement of symptoms

(decrease of the score) was recorded. The latency of P300 also correlated negatively with changes of scores of general psychopathology and overall score of PANSS, however this finding may be valued as contradictory.

When patients where divided into two groups according to their diagnosis, it was noticed, that difference of N2 latency of schizophrenic patients comparing with healthy controls was larger than that in the group of schizoaffective disorder. P300 latency in both groups was abnormal and the differences with control group were statistically significant. The effect of risperidone on parameters of P300 has differed somewhat between the groups. In both groups the tendency of parameters change was the same, but in the case of schizophrenia these changes were not significant, while in schizoaffective disorder group the latency of N2 at Fz, the latency of P300 and duration of RT was significantly shortened, but only after 2 weeks of therapy. After 4 weeks of treatment these changes were insignificant. This suggests that in the case of schizophrenia the neuronal mechanisms at the base of auditory event-related potentials are more impaired and therefore their response to treatment is worse, than in schizoaffective disorder. Similar conclusions were drawn also by other authors, who studied ERPs in patients with schizophrenia and schizoaffective disorders (Ford, 1999; Müller et al., 2001; Jeon and Polich, 2003; Mathalon et al., 2010).

There are only few studies of risperidone action on event-related potential P300. Umbricht et al. in 1999 and Iwanami et al. in 2001 reported that risperidone significantly reduced P300 latency after 4 weeks and 6-9 weeks respectively. Our data seem to support a view that P300 is independent from effects of antipsychotic medication thus serving as a trait marker in schizophrenia (St. Clair et al., 1989, Gonul et al., 2003). However, in our study patients received lower doses of risperidone (2-3 mg/day) whereas in studies of Umbricht and Iwanami higher doses (4-6 mg/day) were administered.

The parameters of P300 of patients who received quetiapine treatment also were abnormal at the baseline when compared with data of healthy controls. These differences were similar to these in common group of risperidone patients – the differences in N2 latency and P300 latency were significant across all electrodes, while the amplitude was significantly decreased in central and parietal areas. However the effect of quetiapine was different than of risperidone. The latency of P300 was

statistically significantly shortened after 2 and 4 weeks of therapy and duration of recognition time became significantly shorter after 4 weeks. This is a sign of increase of speed of information processing in the auditory system. A limitation of this study may be small number of participants, however recent study (Park et al., 2010) also found that after 3 months of quetiapine therapy (number of patients was 20) latencies of both auditory and visual P300 significantly decreased, while amplitude significantly increased. The authors did not found significant correlation between PANSS scores and P300 parameters. The suggestion of this study was that atypical antipsychotic quetiapine may improve some aspects of cognitive domains in patients with schizophrenia.

It may be inferred that quetiapine faster than risperidone enhances disturbed attentional processes in patients with schizoaffective disorder. There are reports that quetiapine has somewhat better effect on clinical symptoms of schizophrenia spectrum disorders than other atypical antipsychotics (Addington et al., 2011), however it is difficult to compare effects of medication on cognitive function with effects on clinical severity of schizophrenia.

The study of antipsychotics have shown that it is difficult to maintain the principle of monotherapy – in order to ensure better therapeutic effect frequently along with atypical antipsychotics there are other, mainly typical antipsychotics, such as haloperidolum, or (particulary in the case of schizoaffective disorder) mood stabilizers added. Anticholinergic drugs also are included to reduce side effects. Therefore it is necessary to consider the introduction of principals of "naturalistic study" in the study of pharmacological effects on ERPs during which the combination of different medications are used for treatment.

4.2. Effect of electroconvulsive therapy on auditory event-related potential P300.

The effect of ECT on the auditory event-related potential P300 was evaluated separately for two groups of patients – group with schizophrenia spectrum disorders and mood disorders. At the baseline almost all parameters of P300 potential in the group of schizophrenia were abnormal – the latencies of N2 and P300 were statistically significantly prolonged and the amplitude was significantly decreased. This is consistent with results of other authors (Frodl et al., 1998; Karaaslan et al., 2003; Vandoolaeghe et al., 1998). It must be noted that ECT is performed only for patients

who are treatment-resistant. This P300 study revealed that cognitive functions of such patients are more disturbed, than patients who received antipsychotic therapy and showed good results of clinical improvement. Patients from the group of mood disorders also were treatment-resistant, but their cognitive functions at the baseline were not so impaired, as in schizophrenia group – only latency of N2 was prolonged across all three electrodes and latency of P300 was abnormal at Fz area.

All studied parameters of P300 potential have changed after the course of ECT – the latencies of N2 and P300 have shortened as well as duration of RT, however only the increase in P300 amplitude was statistically significant. In the group of mood disorders also only one parameter has changed significantly – the amplitude of P300 increased at one electrode – Cz. At the same time latency of P300 and duration of RT tended to increase, but changes were insignificant.

Effect of ECT on the ERP P300 was evaluated only in several studies. It was reported that ECT has heightened the amplitude of P300 in the case of depression (Gangadhar et al., 1993; Ancy J., 1996), in psychotic depression (according to DSM-IV) (Nurminen et al.), 2005) but did not affected latency. The fact that there is increase in amplitude may be attributed to the influence of electrical current on the excitability of cortex. Although data suggests that right after the induced seizure of generalized bioelectrical activity there is temporal increase in seizure threshold (Sackeim et al., 1983, 1987), but longer repetitive stimulation of cortex may enhance recruitment of neurons in bioelectrical response.

It is known that excitability of the cortex is diminished with age (Sackeim et al., 1987; Coffey et al., 1995) and this is taken into account when dosage of ECT stimulation is set. So the all patients who received ECT regardless their diagnosis were divided into two groups according to their age – one group of younger patients (up to 49 years) and a group of older patients (more than 50 years). Results have shown that changes of P300 parameters after the course of ECT were different between the groups. Statistically significant changes in P300 amplitude were recorded only in the group of older patients. This result is somewhat unexpected, but older patients have received higher doses of stimulus energy and this factor could be responsible for the effect in spite of reduced seizure threshold. This circumstance must be taken into account

administering ECT to older persons – it is rational to use upper level of recommended ECT stimulus dosage.

One of the objectives of this work was to search for the correlation between indices of ECT procedure and changes of P300 parameters. Several significant coefficients of correlation were found – changes of recognition time of target stimulus correlated positively with number of ECT procedures and seizure energy index, but negatively with average energy of stimulus of ECT course. Correlation was stronger at Fz electrode. Changes of P300 latency at the same area significantly correlated with number of procedures. Relation of RT with indices of ECT procedure suggests that this P300 parameter needs more attention in the studies of ECT effect on event-related potentials. SEI also needs to be monitored more closely because its correlation with RT was stronger. It may be recommended to record P300 potential not only at the baseline and at the end of the ECT course, but also in the middle of the course (for example, after 2 weeks of ECT). This may help to relate changes of P300 parameters with indices of ECT more precisely.

Evaluation of the correlation between measures of P300 and severity of clinical symptoms of schizophrenia and depression showed that correlation was significant only at the baseline. There was significant positive correlation with P300 latency and negative schizophrenia symptoms. In the group of mood disorders, negatively correlated MADRS scores and P300 amplitude at the parietal area. Meanwhile changes of parameters of P300 potential and changes in clinical symptoms under the influence of ECT did not correlated significantly. All clinical symptoms improved considerably and statistically significantly, while the changes of P300 parameters were not so unambiguous. This may be the reason why the correlation was so weak.

4.3. Effect of metaglosotherapy (MGT) on parameters of auditory P300 potential.

P300 measures at the baseline (pre-treatment) showed that in this group the P300 potential was abnormal as compared with healthy controls – N2, P300 latencies were significantly longer and P300 amplitude was lower. These findings were very similar to abnormalities in ECT group. It may be stressed that participants of MGT group were chronic patients – average duration of illness was 17 years. According to the

specialists, who conducted MGT sessions, patients in the course of MGT gradually became more active, energetic, started to move more easily, eye contact and smiles became present, face expressions more vivid, emotional reactions to each other have appeared. Tension and isolation present at the beginning also diminished. It was evident that patients became more open to the surrounding environment and ready to perceive new information. When measures of P300 were made after MGT all parameters remained abnormal, but statistically significant shortening of P300 potential latency and duration of RT across all three areas was found. These findings suggest that the speed of information processing in auditory system related with allocation of attentional resources and working memory has increased. This effect is somewhat similar to that seen in quetiapine therapy group. However a limitation of this study may be small number of participants.

Interesting results were obtained when correlation of P300 parameters with psychological cognitive tests was studied. At the baseline negative significant correlation between 10 words memorizing test, related with working memory, and P300 latency and duration of RT was found. This may show that the slower is the speed of auditory information processing, the more impaired is working memory. There were also significant cases of correlation between changes of P300 parameters under the influence of MGT and changes of tests scores – negative correlation between changes of P300 latency and duration of RT and changes of digital symbols coding scores. In other words the increase in the speed of information processing was related to increase of speed of psychomotor reactions and memorizing.

It was the first time when the influence of metaglossotherapy on ERP P300 was studied. There are no reports about such studies so it is impossible to compare received results. However MGT can be viewed as a method, which is very close to group of methods of so called “cognitive remediation” or “cognitive enhancement therapy (CET)”. There are no studies of effect of these methods on event-related potentials, but their influence on cognition, evaluated with neuropsychological tests is being researched. It was reported that cognitive remediation increase the speed of information processing and enhance attentional processes (Wykes ir kt. 2002; Wexler ir Bell, 2005; Wexler, 2007; Hogarty et al., 2004, 2006). It appears that many positive changes in cognition of schizophrenic patients induced by cognitive remediation were sustained at least 1 year

after the treatment (Hogarty et al., 2004, 2006; Turkington et al., 2008). So it may be concluded that methods of nonpharmacological treatment of cognitive functions are productive enhancing disturbed cognition in schizophrenia patients. The results of P300 measures in this work provide additional support for this conclusion. Nevertheless, to state that these positive changes of P300 are due particularly to language learning, but not to simple training of such separate cognitive processes as attention, memory, social cognition is at this stage of research impossible.

Summarizing the results of this work it may be said that P300 is a sensitive measure of disturbed cognitive functions, such as attention and working memory, in patients with schizophrenia – parameters of P300 potential were more abnormal (in spite of inconsistent correlation between PANSS values and P300 measures) in the group of treatment-resistant patients, who were treated with ECT and the MGT group of chronic schizophrenia patients.

As for the results of study of correlation between P300 measures and clinical symptoms it was found that relation between PANSS scores and processes of auditory information processes was inconsistent. Thus, when all data of PANSS (the number of patients whose symptoms were evaluated was 26) were assessed in relation to measures of P300 only one statistically significant, but mild coefficient of correlation was found – there was negative correlation between duration of recognition time of target stimulus and positive symptoms scale values. Other researchers also reported similar lack of consistent correlation. This was found not only studying P300 potential (Laurent et al., 1999; Mathalon ir kt., 2010), but also mismatch negativity (MMN) (Javitt et al., 1995; Kirino and Inoue, 1999; Umbricht and Krljes, 2005). There was no correlation found between cognitive tests, evaluating verbal memory and learning, verbal fluency, attention, short-term memory, and PANSS scores (Akdede et al., 2006). Therefore it is reasonable in studies of ERPs and the effect of different treatment methods on them in psychiatric practice to use cognitive tests, while clinical symptoms scales may be used for evaluation of severity of psychiatric illness and its changes.

CONCLUSIONS

1. P300 potential of patients from all studied groups was abnormal as compared with healthy controls, only in the group of mood disorders differences were less expressed than in patients with schizophrenia spectrum disorders.
2. 4 weeks of therapy with risperidone did not have statistically significant effect on P300 parameters of patients with schizophrenia.
3. There was temporary positive effect of risperidone on P300 parameters in patients with schizoaffective disorder.
4. Therapy with antipsychotic quetiapine had positive effect on cognitive functions of patients with schizoaffective disorder.
5. Electroconvulsive therapy had positive influence on the amplitude of P300 potential, its increase in the group of older patients was more considerable and changes of parameters of P300 potential correlated with number of procedures of ECT and invoked seizure energy index.
6. The speed of processing of information in auditory system of patients with schizophrenia has increased after course of metaglossotherapy.

SANTRAUKA (Summary in Lithuanian)

Su įvykiu susiję sukeltieji galvos smegenų potencialai (SĮSP) leidžia įvertinti kai kurias kognityviąsias funkcijas. Jie nuo pat sukūrimo pradžios yra sėkmingai taikomi ir psichikos sutrikimų tyrimuose. SĮSP neinvaziškumas, objektyvumas, saugumas leidžia juos taikyti kognityviųjų funkcijų pokyčių, sukeltų medikamentinio gydymo ar kitos nemedikamentinės terapinės procedūros, įvertinimui. Naujos kartos antipsichotikai, skirti šizofrenijos simptomų gydymui, efektyviai mažina psichozės simptomus, turi mažiau pašalinių reiškinių, negu jų pirmtakai tipiniai antipsichotikai, bet jų įtaka kognityviosioms paciento funkcijoms nėra patenkinama. Be to, dar nėra pakankamai ištirtas jų poveikis informacijos apdorojimo procesams galvos smegenyse. Todėl naujų antipsichotikų poveikio P300 potencialo parametrams tyrimas yra svarbus, norint gauti kuo išsamesnius duomenis apie informacijos apdorojimo procesus galvos smegenyse naujos kartos atipinių antipsichotikų poveikyje. Greta medikamentinių gydymo metodų taikomi ir kiti metodai, kurie ypač tinka esant rezistentiškumui gydymui vaistais. Vienas tokių efektyvių terapijos metodų yra elektros impulsų terapija (EIT). Jos metu, leidžiant impulsinę elektros srovę per smegenis, iššaukiamas generalizuotas bioelektrinio aktyvumo iškrūvis. Jo poveikyje smegenyse ir neuronuose atsiranda įvairių fiziologinių pokyčių, kurie duoda teigiamą terapinį efektą. EIT įtaka kognityviosioms paciento funkcijoms ištirta mažai. Taip pat netirtas EIT procedūros parametrų ryšys su kognityviųjų sukeltųjų potencialų parametrų kitimu. Vaistų teigiamas poveikis kognityviosioms funkcijoms nėra pakankamas, todėl ieškoma kitų būdų pažintinėms funkcijoms gerinti. Alternatyva šiuo atveju gali būti taip vadinamas kognityvusis gydymas. Tai gali būti įvairių pratimų, skirtų atskirų kognityviųjų funkcijų treniravimui, rinkinys, taip pat ir kompiuterizuoti testų variantai. Vienas įdomesnių tokio poveikio variantų yra metaglosoterapija – nežinomos, neutralios kalbos mokymas, kuris, manoma, gali padėti ilgai šizofrenija sergančiam pacientui atkurti deramą ryšį su realybe, iš naujo suformuluoti kitos kalbos konstrukcijomis sveikiems žmonėms įprastas sąvokas. Metaglosoterapijos poveikis kognityviosioms funkcijoms iš viso nežinomas, nes niekada nebuvo tirtas.

Pagrindinis darbo tikslas buvo įvertinti informacijos apdorojimo klausos sistemoje kitimą atipinių antipsichotikų risperidono ir kvetiapino poveikyje ir nemedikamentinių terapijos metodų - elektros impulsų terapijos bei metaglosoterapijos -

poveikyje taikant su įvykiu susijusio potencialo P300 skaitmeninio registravimo ir kiekybinės analizės metodus. Klausos sukeltas P300 potencialas buvo registruojamas taikant „atsitiktinio įvykio“ principą trimis elektrodais (Fz, Cz ir Pz). Buvo matuojami 4 sukeltojo potencialo P300 parametrai: N2 latencija, P300 latencija, P300 amplitudė ir reikšmingo dirgiklio atpažinimo laikas. Ištirtos šešios skirtingos grupės pacientų (viso 85 žmonės). Darbo rezultatai parodė, kad SĮSP parametrai yra jautrūs informacijos apdorojimo klausos sistemoje procesų pažeidimo šizofrenijos spektro sutrikimų atveju rodikliai. Didesnę teigiamą įtaką klausos sukeltajam potencialui P300 turėjo atipinis antipsichotikas kvetiapinas. Nemedikamentiniai psichikos sutrikimų gydymo metodai nenusileidžia efektyvumu gerinant pacientų kognityviąsias funkcijas medikamentinei terapijai atipiniais antipsichotikais.

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