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Evaluation of the effectiveness of rehabilitation of people diagnosed with schizophrenia using clinical tools, psychological tests, QEEG, and the brain-derived neurotrophic factor (BDNF)

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Summary

Aim. The aim of the study was to evaluate the level of cognitive and social functioning in two groups of schizophrenia patients using clinical tools, psychological tests, QEEG, and changes in the brain-derived neurotrophic factor (BDNF) activity in subjects' serum.

Material and methods. Randomly selected men diagnosed with schizophrenia were enrolled in the study and divided into two groups. Gr. 1 was formed by patients who did not undergo a structured rehabilitation program, while Gr. 2 was formed by patients undergoing standard rehabilitation, as provided in the program of the Psychiatric Rehabilitation Unit. Both groups underwent a comparative analysis of demographic parameters and based on: PANSS, AIS, GSES, and BCIS, psychological tests CTT-1, CTT-2, d2, QEEG, and changes in blood BDNF levels. To assess the effect of rehabilitation, the results obtained in both groups were compared after 12 weeks and their analysis was performed in accordance with assumptions for the experimental project. The study presents research hypotheses and pre-test and post-test comparisons of the groups, on the basis of selected research tools.

Results. The data obtained in measurement 1 indicate that both groups did not differ significantly in terms of: age, education, place of residence, treatment at outpatient facilities, medicines taken, and suicide attempts. Differences concerned: marital status, children, number of hospitalizations, and employment status. Furthermore, no significant differences were found for the studied groups concerning: serum levels of the brain-derived neuro-

trophic factor, values obtained on the PANSS, AIS, and GSES, and alpha/theta, theta/beta and theta/SMR ratios. The analyses performed in measurement 2 indicate that structured rehabilitation influences reduce negative symptoms, cause an increase in BDNF levels, cause an improvement in cognitive and social functioning and positively influence the perception speed and accuracy.

Conclusions. The positive effect of structured rehabilitation influences allows to say that rehabilitation represents a necessary part of the comprehensive psychiatric treatment and should already be implemented during the first episode of the illness.

Introduction

Schizophrenia is one of many mental illnesses of multi-factor pathogenesis and frequently a recurrent course [1]. The productive (positive) symptoms predominate mainly during the period of illness exacerbation, while the deficit (negative) symptoms prevail during the remission. Both positive and negative symptoms result from the disrupted activity of different areas of the brain [2]. Published reports indicate an important role of the frontal and temporal regions, limbic and medial structures, and of the basal ganglia [1, 3, 4]. Dysfunctions in the pre-frontal region mainly influence the processes associated with working memory, focusing, emotions, and executive functions [1, 5–8] that significantly affect functioning of patients and their quality of life [1, 5, 6, 9–11].

Schizophrenia, as an illness with a varying course, requires multidirectional rehabilitation influences. However, regular pharmacotherapy remains the basic form of treatment [12, 13]. Non-pharmacological interventions involve a wide range of effects and take many dimensions into account: family, professional and social. Both pharmacotherapy and the auxiliary stage are important, as they divide the whole treatment process into two periods: early and delayed [12, 14]. At the early stage, mainly the acute symptoms of the illness are eliminated and disrupted social relations are restored [12–14]; while at the later stage, the diagnosed dysfunctions are compensated, the scope of help is determined, and the social activity and disrupted functions are improved. Both periods are important, as they form a consistent model of treatment [14].

An individual therapeutic program combines various forms of therapy: neurological rehabilitation, psychoeducation and psychotherapy. The rehabilitation process, through work, physical and cognitive activity, plays an important role in recovery. Each form of structured activity is important, as it influences the patient's cognitive and social functioning [15]. This effect is demonstrated in this paper, using clinical and psychological tests and parameters of neuronal activity – BDNF and quantitative EEG (so-called QEEG).

Aim

The aim of this randomized study was a comparison of two groups of patients – men diagnosed with schizophrenia (in the remission phase). One group included

patients who did not undergo a structured rehabilitation program, while the second group included patients undergoing a standard rehabilitation program provided by the Psychiatric Rehabilitation Unit. The inclusion criteria were as follows: patient's consent, clinical diagnosis of schizophrenia (DSM-5), patient's age within a range of 18–50 years, dextrality, lack of neurological diseases (active and in the past), as well as excluded mental disability, dementia, and alcohol addiction.

Both groups were compared in terms of demographic parameters, and measurements were performed twice on the basis of CTT-1, CTT-2, and d2 tests, PANSS, AIS, GSES, and BCIS scales, BDNF serum levels, and QEEG. It was assumed that there were differences in cognitive and social functioning between groups 1 and 2, which would be shown by research methods and tools used in the study.

According to a hypothesis adopted in the study, rehabilitation influences improve cognitive and social functioning in people diagnosed with schizophrenia, and the selected research tools would prove:

- reduction in cognitive deficits (CTT-1, CTT-2 and d2 tests, BDNF);
- reduction in positive (P) and negative (N) symptoms (PANSS scale);
- improvement in the social adaptation (AIS, GSES and BCIS scales);
- positive effect on the brain function (QEEG), wave ranges and amplitudes, including attention measure (theta/beta) and concentration ratio (theta/SMR).

Material

Men diagnosed with schizophrenia were enrolled in the study and divided into two groups. Group 1 (19 people) consisted of patients hospitalized at the 2nd Clinic of Psychiatry, Medical University of Lublin, for which no structured rehabilitation influence was applied, while group 2 (26 people) included patients staying at the Psychiatric Rehabilitation Unit, Neuropsychiatric Hospital, Lublin. The patients from group 2 underwent standard influences in accordance with the Unit program. The program included several types of training: hygienic, medicinal, budget, relaxing, practical skills, social and communication skills, additional activities (sports, arts and social activities), as well as psychological assistance. For each patient, a schedule of activities was based on their existing deficits and arranged by the personnel employed at the Unit (a doctor, a psychologist, and a nurse). Each patient was obliged to actively participate in the complete series of activities in accordance with the arranged rehabilitation schedule.

The comparative demographic analysis of both groups showed that there were no significant differences in terms of age, education, place of residence, treatment at outpatient facilities, medicines taken, and suicide attempts. The mean age of subjects was 38 years (M = 38.16; SD = 10.78) in group 1, and 36 years (M = 36.38; SD = 8.86) in group 2. In group 1, 3 people had primary, 6 – vocational, 7 – secondary, and 3 – higher education. In group 2, 4 people had primary, 9 – vocational, 9 –

secondary, and 4 – higher education. In group 1, 7 people lived in large cities (over 100,000 inhabitants), 5 people lived in smaller towns (below 100,000 inhabitants), and 7 people lived in rural areas. In group 2, 4 people lived in large cities, 10 people lived in smaller towns, and 11 people lived in rural areas. All subjects took atypical neuroleptics, including 3 patients in group 2 taking them in the form of intramuscular injections. Both, subjects in group 1 (15 people) and group 2 (16 people) declared an irregular treatment at an outpatient clinic and negated suicide attempts (group 1 – 15 people, group 2 – 17 people).

Differences between the groups concerned: marital status, children, number of hospitalizations, and employment status. In group 2, the number of single patients was twice as high (23 people), and those with children was three times lower (1 child) than in group 1. In group 2, the mean number of hospitalizations ($M = 8.00$) was twice as high as in group 1 ($M = 3.53$). The sources of income in group 2 were mainly the disability benefit (16 people) or temporary work (5 people). The remaining people were supported by Social Welfare Centers (3 people) or their families (2 people). The sources of income in group 1 were also the disability benefit (6 people) and social welfare (3 people), seven subjects were supported by their families, while 3 patients were employed.

Methods

In accordance with the experiment assumptions, the patients enrolled in the study were examined twice. The first examination was associated with qualification and patient's consent; the second was performed 12 weeks after the enrolment of the patients into the program. The comparative analysis was performed on the basis of tests, scales, blood samples, and QEEG parameters (Bioethics Committee approval no. KE-0254/35/2016). The study used:

1) diagnostic CTT test (D'Elia et al. [16]) to analyze the frontal dysfunction – its version CTT-1 determined visual performance and psychomotor speed (alternate joining of colored numbers in a string from 1 to 25), the CTT-2 version determined performance skills and working memory (alternate joining of numbers with simultaneous selection of a color sequence in a string from 1 to 25);
2) d2 test of attention (Brickenkamp [17]) analyzing the speed (amount of material processed in a specific time), quality (work precision and errors made) and persistence indicating features of behavior during work (irritation, stability of work or lack of it, discouragement, fatigue); the level of concentration was a result of interaction of these behaviors, it was an outcome of the coordination of the stimulus and the control [17];
3) PANSS (Kay, Opler and Fiszbein [18]) evaluating mental disorders in schizophrenia (positive, negative and general symptoms);
4) Beck Cognitive Insight Scale (BCIS [19];
5) Acceptance of illness scale (AIS) (Felton, Revenson and Hinrichsen [20]);

6) Self-efficacy scale (GSES) (Schwarzer, Jerusalem and Juczyński) [20];
7) quantitative EEG (so-called QEEG), in terms of wave amplitudes and frequency ratios using the apparatus from Elmiko [21].

The laboratory parameter of the brain-derived neurotrophic factor (BDNF) was determined following blood sampling into a clot tube using a non-contact method. This marker was considered important because, as an indicator of synergism between the central and peripheral nervous systems, it may justify the effectiveness of rehabilitation interventions [22]. BDNF serum levels were determined using the immunoenzymatic technique ELISA (Human BDNF ELISA kit, R&D Systems). The neuropsychological evaluation was performed by a psychologist, and BDNF levels were determined by a laboratory diagnostician.

The obtained results were statistically analyzed using Statsoft STATISICA software, and the distribution of significance of differences was evaluated with the non-parametric Mann-Whitney *U* test. The effect size was analyzed using the Cohen's coefficient (*r*), where $r \geq 0.5$, $r \geq 0.3$ and $r \geq 0.1$ represent large, medium and small effect, respectively.

Results

In order to verify the assumptions adopted in our studies, the results obtained for groups 1 and 2 during examinations 1 and 2, were compared.

Table 1. **Comparison of mean results obtained on the PANSS**

PANSS	Group 1 (N=19)					Group 2 (N=26)				p^3 p^4	Cohen's effect size r
	Examination number	M	SD	p^1	Cohen's effect size r	M	SD	p^2	Cohen's effect size r		
PANSS–POS	1	9.95	2.32	0.023	0.32	8.92	2.68	0.001	0.52	0.273	0.16
	2	9.47	2.87			7.92	2.54			0.123	0.23
PANSS–NEG	1	15.16	3.70	0.001	0.57	14.58	4.54	0.009	0.33	0.899	0.02
	2	17.58	4.39			13.54	5.18			0.010	0.38
PANSS–GEN	1	25.89	4.25	0.001	0.51	26.38	6.28	0.009	0.33	0.473	0.11
	2	28.37	4.59			24.88	6.53			0.051	0.29
PANSS–TOT	1	51.00	9.13	0.001	0.52	49.92	12.40	0.002	0.41	0.954	0.01
	2	55.42	10.71			46.35	13.17			0.012	0.37

p^1 – comparison of examination 1 and 2 in group 1; p^2 – comparison of examination 1 and 2 in group 2; p^3 – comparison of group 1 results with group 2 results in examination 1; p^4 – comparison of group 1 results with group 2 results in examination 2

PANSS–POS – positive items total; PANSS–NEG – negative items total; PANSS–GEN – general items total; PANSS–TOT – total score

The *U* test results show statistically significant differences in the PANSS–NEG levels (group 1: *M* = 17.6; *SD* = 4.4 vs. group 2: *M* = 13.5; *SD* = 5.2) and the PANSS–TOT (group 1: *M* = 55.4; *SD* = 10.7 vs. group 2: *M* = 46.4; *SD* = 13.2). The increase in negative symptoms in subjects from group 2 was lower than in subjects from group 1.

Table 2. **Comparison of mean results obtained for AIS, GSES and BCIS scales**

Analyzed scale	Group 1 (N=19)					Group 2 (N=26)				p^3 p^4	Cohen's effect size r
	Examination number	M	SD	p^1	Cohen's effect size r	M	SD	p^2	Cohen's effect size r		
AIS	1	29.53	7.07	0.093	0.30	25.96	8.77	0.228	0.15	0.129	0.22
	2	25.00	7.83			31.26	7.07			0.01	0.38
GSES	1	32.00	6.22	0.267	0.14	30.15	5.76	0.201	0.16	0.244	0.17
	2	28.69	6.16			32.42	6.29			0.03	0.32
BCIS – Self-reflectiveness	1	21.95	5.62	0.388	0.07	21.15	4.47	0.126	0.22	0.872	0.03
	2	22.12	4.96			21.10	7.79			0.68	0.06
BCIS – Self-confidence	1	17.47	3.69	0.371	0.08	21.15	4.47	0.433	0.03	0.022	0.34
	2	14.77	3.29			16.74	5.64			0.03	0.33

p^1 – comparison of examination 1 and 2 in group 1; p^2 – comparison of examination 1 and 2 in group 2; p^3 – comparison of group 1 results with group 2 results in examination 1; p^4 – comparison of group 1 results with group 2 results in examination 2

The *U* test results show statistically significant differences in illness acceptance, AIS (group 1: *M* = 25; *SD* = 7.8 vs. group 2: *M* = 31.3; *SD* = 7.1), self-efficacy, GSES (group 1: *M* = 28.7; *SD* = 6.2 vs. group 2: *M* = 32.4; *SD* = 6.3) and self – confidence, BCIS (group 1: *M* = 14.8; *SD* = 3.3 vs. group 2: *M* = 16.7; *SD* = 5.6). The data indicate that in the subjects from group 2 the rehabilitation interventions led to an improvement in their social functioning.

Table 3. **Comparison of mean results obtained for the brain-derived neurotrophic factor**

Neurotrophic factor	Group 1 (N = 19)					Group 2 (N = 26)				p^3 p^4	Cohen's effect size r
	Examination number	M	SD	p^1	Cohen's effect size r	M	SD	p^2	Cohen's effect size r		
BDNF	1	47.89	8.61	0.001	0.54	48.23	14.87	0.077	0.20	0.721	0.05
	2	36.37	10.25			50.92	14.76			0.000	0.58

p^1 – comparison of examination 1 and 2 in group 1; p^2 – comparison of examination 1 and 2 in group 2; p^3 – comparison of group 1 results with group 2 results in examination 1; p^4 – comparison of group 1 results with group 2 results in examination 2

The *U* test results show statistically significant differences in mean values for the brain-derived neurotrophic factor (BDNF) results (group 1: $M = 36.4$; $SD = 10.3$ vs. group 2: $M = 50.9$; $SD = 14.7$). The analyses indicate that the rehabilitation interventions resulted in an increase in the mean values for the BDNF in group 2.

Table 4. **Comparison of mean results obtained for CTT-1, CTT-2 and d2 tests**

CTT-1, CTT-2, d2 test	Group 1 (N = 19)					Group 2 (N = 26)				p^3 p^4	Cohen's effect size r
	Examination number	M	SD	p^1	Cohen's effect size r	M	SD	p^2	Cohen's effect size r		
CTT-1/visual attention – simple sequence	1	56.1	26.1	0.167	0.22	57.04	25.8	0.027	0.38	0.58	0.08
	2	50.4	24			50.1	24			0.95	0.01
CTT-2/visual attention – alternate sequence	1	117.4	55.3	0.018	0.48	116.9	43.6	0.036	0.35	0.62	0.08
	2	102.3	51.7			101.8	43.3			0.47	0.11
CTT/ disruption ratio	1	1.2	0.6	0.391	0.06	1.2	0.8	0.355	0.07	0.88	0.02
	2	1.2	0.7			1.1	0.6			0.62	0.07
d2 WZ/ operating speed	1	348.8	88.4	0.015	0.50	309.1	105.2	0.440	0.03	0.35	0.14
	2	377.8	127.1			303.7	113.4			0.02	0.34
d2%B/ mistakes	1	39.4	37.8	0.026	0.45	18.4	10.7	0.037	0.35	0.00	0.57
	2	31.2	27.3			15.8	6.8			0.00	0.60
d2 WZ-B/ perception ability	1	236.4	115.6	0.024	0.45	281.1	100.6	0.222	0.15	0.33	0.14
	2	256.8	129.4			285.2	109.3			0.36	0.14
d2 ZK/ ability to concentrate	1	131.6	95.2	0.120	0.27	103.1	49.5	0.072	0.29	0.71	0.05
	2	144.4	123.1			108.8	46.8			0.88	0.02

p^1 – comparison of examination 1 and 2 in group 1; p^2 – comparison of examination 1 and 2 in group 2; p^3 – comparison of group 1 results with group 2 results in examination 1; p^4 – comparison of group 1 results with group 2 results in examination 2

The *U* test results disclose statistically significant differences in d2%B test indicating an increase in the perception accuracy (group 1: $M = 31.2$; $SD = 27.3$ vs. group 2: $M = 15.8$; $SD = 6.8$) and work speed (group 1: $M = 377.8$; $SD = 127.1$ vs. group 2: $M = 303.7$; $SD = 113.4$). The improvement is observed in the subjects from group 2.

Table 5. **Comparison of mean results obtained for QEEG/frequency ratio**

Frequency ratio – Hz	Group 1 (N = 19)					Group 2 (N = 26)				p^3 p^4	Cohen's effect size r
	Examination number	M	SD	p^1	Cohen's effect size r	M	SD	p^2	Cohen's effect size r		
QEEG Fzdelta/theta	1	1.66	0.49	0.042	0.28	1.57	0.47	0.465	0.01	0.62	0.07
	2	1.92	0.61			1.49	0.47			0.03	0.31
QEEG Fztheta/alpha	1	1.36	0.27	0.001	0.43	1.44	0.56	0.132	0.16	0.99	0.01
	2	1.53	0.30			1.44	0.59			0.26	0.16
QEEG Fzalpha/SMR	1	1.70	0.25	0.039	0.29	2.10	0.38	0.121	0.16	0.00	0.53
	2	1.87	0.39			1.99	0.53			0.07	0.26
QEEG Fz SMR/beta	1	0.90	0.10	0.192	0.14	0.95	0.10	0.173	0.13	0.029	0.32
	2	0.87	0.15			0.90	0.19			0.13	0.23
QEEG Fz beta/Beta2	1	0.76	0.09	0.431	0.03	0.82	0.12	0.422	0.03	0.13	0.23
	2	0.73	0.10			0.79	0.21			0.15	0.21
QEEG Fztheta/beta	1	2.14	0.61	0.016	0.35	2.86	1.22	0.361	0.05	0.02	0.36
	2	2.46	0.79			2.76	1.09			0.38	0.13
QEEG Fztheta/SMR	1	2.34	0.62	0.000	0.54	3.01	1.25	0.255	0.09	0.04	0.30
	2	2.79	0.64			2.89	1.13			0.77	0.04
QEEG Fzalpha/theta	1	0.74	0.12	0.019	0.34	0.79	0.26	0.102	0.18	0.83	0.03
	2	0.67	0.14			0.73	0.26			0.22	0.18
QEEG Fz SMR/beta2	1	0.68	0.13	0.382	0.05	0.78	0.15	0.395	0.04	0.03	0.34
	2	0.64	0.15			0.80	0.30			0.02	0.36
QEEG Fzalpha/beta	1	1.53	0.29	0.024	0.32	1.99	0.34	0.051	0.23	0.00	0.59
	2	1.66	0.48			1.87	0.48			0.04	0.30
QEEG Fz beta/alpha	1	0.68	0.12	0.089	0.22	0.52	0.10	0.232	0.10	0.00	0.59
	2	0.71	0.45			0.50	0.13			0.00	0.43
QEEG Cz delta/theta	1	1.54	0.74	0.167	0.16	1.28	0.27	0.363	0.05	0.24	0.17
	2	1.65	0.66			1.22	0.37			0.02	0.34
QEEG Cztheta/alpha	1	1.29	0.35	0.103	0.21	1.21	0.46	0.058	0.22	0.10	0.24
	2	1.35	0.27			1.22	0.53			0.10	0.24
QEEG Czalpha/SMR	1	1.74	0.33	0.186	0.14	2.09	0.47	0.363	0.05	0.15	0.21
	2	1.83	0.39			2.08	0.62			0.03	0.33

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QEEG Cz SMR/beta	1	0.92	0.14	0.397	0.04	0.94	0.09	0.230	0.10	0.26	0.17
	2	0.86	0.13			0.89	0.19			0.15	0.21
QEEG Cz beta/beta2	1	0.79	0.18	0.448	0.002	0.82	0.13	0.267	0.09	0.28	0.16
	2	0.74	0.10			0.82	0.24			0.05	0.28
QEEG Cztheta/ beta	1	2.09	0.85	0.082	0.23	2.35	0.92	0.129	0.16	0.22	0.18
	2	2.13	0.57			2.39	0.94			0.33	0.14
QEEG Cztheta/ SMR	1	2.23	0.69	0.020	0.34	2.49	0.98	0.177	0.13	0.25	0.17
	2	2.45	0.49			2.49	0.95			0.94	0.01
QEEG Czalpha/theta	1	0.79	0.16	0.204	0.13	0.92	0.28	0.032	0.26	0.11	0.24
	2	0.76	0.15			0.86	0.28			0.06	0.27
QEEG Cz SMR/beta2	1	0.75	0.31	0.500	0.01	0.77	0.15	0.404	0.03	0.10	0.25
	2	0.65	0.14			0.79	0.28			0.01	0.36
QEEG Czalpha/beta	1	1.57	0.37			1.96	0.42	0.371	0.05	0.01	0.45
	2	1.63	0.46	0.066	0.24	1.95	0.56			0.01	0.35
QEEG Cz beta/alpha	1	0.67	0.16	0.107	0.20	0.53	-0.13	0.289	0.08	0.01	0.43
	2	0.68	0.33			0.49	0.13			0.00	0.43

p^1 – comparison of examination 1 and 2 in group 1; p^2 – comparison of examination 1 and 2 in group 2; p^3 – comparison of group 1 results with group 2 results in examination 1; p^4 – comparison of group 1 results with group 2 results in examination 2

Fz – frontal area of the brain; Cz – central area of the brain

The *U* test results show statistically significant differences in the delta/theta frequency ratio in the Fz region (group 1: $M = 1.9$; $SD = 0.6$ vs. group 2: $M = 1.5$; $SD = 0.5$). An increase in mean results for this ratio in group 1 implies problems with recalling information and limited control over a reaction to a stimulus. Statistically significant differences also occur for the SMR/beta2 ratio (group 1: $M = 0.6$; $SD = 0.2$ vs. group 2: $M = 0.8$: $SD = 0.3$). Its increase in group 2 indicates a reduction in tension and stress in the subjects.

A statistically significant difference was also noted for the alpha/beta ratio (group 1: $M = 1.7$; $SD = 0.5$ vs. group 2: $M = 1.9$; $SD = 0.5$), which decreased in group 2. Its reduction indicates a slight improvement in logical thinking and problem solving. Analogical differences for delta/theta, SMR/beta2 and alpha/beta ratios also concern the Cz region. The groups did not differ in their attention ratio theta/beta and in their concentration ratio theta/SMR.

Table 6. **Comparison of mean results obtained for QEEG /amplitude**

Wave amplitude	Group 1 (N = 19)					Group 2 (N = 26)				p^3 p^4	Cohen's effect size r
	Examination number	M	SD	p^1	Cohen's effect size r	M	SD	p^2	Cohen's effect size r		
QEEG Fzdelta	1	24.38	8.75	0.03	0.31	30.24	11.11	0.395	0.04	0.06	0.10
	2	27.06	9.85			28.53	12.01			0.52	0.10
QEEG Fztheta	1	14.93	4.24	0.04	0.28	20.31	9.06	0.310	0.07	0.013	0.20
	2	16.35	4.81			19.24	7.75			0.17	0.20
QEEG Fzalpha	1	10.8	2.67	0.148	0.17	14.52	4.9	0.297	0.07	0.001	0.35
	2	10.68	3.27			13.49	4.17			0.01	0.35
QEEG Fz SMR	1	5.96	1.54	0.048	0.27	7.07	2.61	0.490	0.01	0.06	0.37
	2	5.53	1.47			6.55	1.94			0.01	0.37
QEEG Fz beta	1	6.6	1.27	0.015	0.35	7.38	2.2	0.415	0.03	0.19	0.36
	2	5.92	1.38			7.05	2.25			0.01	0.36
QEEG Fz beta2	1	8.8	1.51	0.005	0.42	9.20	2.00	0.410	0.03	0.78	0.21
	2	7.62	1.88			8.65	3.02			0.15	0.21
QEEG Cz delta	1	21.18	8.9	0.374	0.05	22.35	7.52	0.138	0.15	0.29	0.04
	2	20.77	7.26			20.95	9.62			0.8	0.04
QEEG Cztheta	1	14.89	4.14	0.500	0.01	17.24	5.96	0.144	0.17	0.14	0.15
	2	15.16	4.49			17.13	6.81			0.32	0.15
QEEG Czalpha	1	11.4	3.09	0.056	0.26	14.66	3.15	0.347	0.05	0.002	0.39
	2	11.20	3.38			14.38	4.57			0.00	0.39
QEEG Cz SMR	1	6.29	1.6	0.015	0.35	7.13	1.78	0.129	0.16	0.14	0.34
	2	5.77	1.43			6.73	2.04			0.02	0.34
QEEG Cz beta	1	6.84	1.4	0.011	0.37	7.54	1.83	0.191	0.12	0.28	0.33
	2	6.24	1.24			7.20	2.21			0.02	0.33
QEEG Cz beta2	1	9.0	1.47	0.009	0.39	9.23	2.32	0.091	0.18	0.99	0.17
	2	7.91	1.67			8.60	2.75			0.26	0.17

p^1 – comparison of examination 1 and 2 in group 1; p^2 – comparison of examination 1 and 2 in group 2; p^3 – comparison of group 1 results with group 2 results in examination 1; p^4 – comparison of group 1 results with group 2 results in examination 2

Fz – frontal area of the brain; Cz – central area of the brain

The *U* test results show statistically significant differences in the alpha wave amplitude in the Fz region (group 1: $M = 10.7$; $SD = 3.3$ vs. group 2: $M = 13.5$; $SD = 4.2$). A reduction in the mean values in group 1 implies problems with cognitive functioning.

A statistically significant difference was also noted for the SMR wave amplitude (group 1: $M = 5.5$; $SD = 1.5$ vs. group 2: $M = 6.6$; $SD = 1.9$). A reduction in the mean values of the SMR wave in group 1 indicates a decrease in the subjects' activity. A statistically significant change was also noted for the beta wave amplitude (group 1: $M = 5.9$; $SD = 1.4$ vs. group 2: $M = 7.1$; $SD = 2.3$). A reduction in the mean values of beta waves in group 1 indicates a weaker external orientation in the subjects. Analogical differences in the range of amplitudes of alpha, SMR and beta waves concern the Cz region.

Discussion

Results of the first phase of the experiment (examination 1) show no statistically significant differences between the studied groups of patients. Initially, both groups of patients do not differ as regards the average values in the PANSS, AIS and GSES scales, levels of the brain-derived neurotrophic factor, and mean values of alpha/theta, theta/beta and theta/SMR ratio. The second phase of the research (examination 2) reveals statistically significant differences in group 2, in which a standard psychiatric rehabilitation program was applied. Statistically significant differences concern the d2 test, which indicates improvement in perception accuracy (d2%B) and speed of work (d2WZ), and the PANSS, which reveals reduced intensity of negative symptoms. The obtained results correspond to the reports of other authors who indicate the positive effects of rehabilitation focused on shaping the abilities after 4 weeks only, which was confirmed by the results of psychological tests and the PANSS [23, 24].

In group 2, there was also a statistically significant growth in the BDNF level, which corresponds to the results of Kim et al. [25]. The authors also observed the increased level of BDNF in patients diagnosed with schizophrenia as a result of physical exercises three times a week for 3 months. Additionally, they observed positive correlation between the increased level of BDNF and the parameters of the cardiovascular system of the studied subjects [22, 25]. The data obtained from the experiment also correspond to the results obtained by Mattson et al. [26], and Mannerick and Zorumski [27], according to which the energy transformations cause a cascade of biochemical processes, production of neurotransmitters, and increased synthesis of BDNF [22]. The obtained results are also in line with the findings of Mabuchi et al. [28], and Powers and Jackson [29], according to which the activity of muscle cells and neurons through the induction of the inflow of sodium and calcium ions causes improved transport of electrons, activation of metabolic processes, proteins and enzymes production, transcription stimulation, and increased number of vesicles containing neurotransmitters [22]. The results show that changes in the concentration of neurotrophic factor may be an indicator of the synergism of the central and peripheral nervous systems, and the increased concentration of BDNF determined by physical activity and neuromodulatory effect of rehabilitation may prove its efficiency.

The results obtained by patients from group 2, concerning the values in the following scales: Acceptance of Illness Scale (AIS), General Self-efficacy Scale (GSES) and

Beck Cognitive Insight Scale (BCIS), are also statistically significant. The analyses show that the social functioning of those persons is also improved due to rehabilitation. The results correspond to the research by Schaub et al. [30] who claim that the insight and own effectiveness constitute important moderating factors of social behavior of persons suffering from schizophrenia.

An interesting result is the statistically significant difference in the values of frequency factors in the Fz region. The increased SMR/beta2 ratio in group 2 proves a reduction of tension, reduced anxiety and stress, and the reduced alpha/beta ratio indicates a slight improvement in thinking. Both groups demonstrate a similar alpha/theta ratio associated with mood, which, according to Crumlish et al. [31], is a reaction to the illness and cognitive biases [21]. The author claims that the distorted reception of information depends on psychopathological symptoms that cause concentration and attention deficiency, which is confirmed by the results of our research – theta/beta attention ratio and theta/SMR concentration ratio.

At present, there are only few publications that analyse the quantitative EEG (so-called QEEG) assessment of brain activity in persons with diagnosed schizophrenia under different impacts. There is a possibility that such a connection exists. Papers by Gruzelier and Gruzelier et al. [32–35], who analyzed attention, concentration and memory in a group of artists on the basis of the alpha/theta, SMR/theta and SMR/beta2 protocols, are an example of such works. They demonstrated that active trainings improve cognitive processes in musicians and increase their artistic capabilities. They obtained similar results when examining healthy subjects using SMR/beta1 protocol. They also proved a positive effect of the therapy on self-control and reflective action (SMR) and on concentration and decision making in problems solving (beta1). The results obtained by Gruzelier et al. were confirmed also by many other researchers. Therefore, it seems likely that the use of specific training protocols in patients with schizophrenia may also improve their cognitive processes [36–41].

The results presented in this paper have also been confirmed by scientific works in which the improvement of cognitive processes is proved by the event-related potentials (ERP). Kariofillis et al. [42] studied the influence of cognitive training (hearing and visual and spatial training) on the potentials induced in patients diagnosed with schizophrenia. They carried out a computer training for 2 weeks and analyzed the potentials induced in odd-ball paradigm before the training, after 2 weeks of training, and after 2 months. In both studied groups they confirmed the reduction of P2 wave latency after the training, and in the follow-up study. According to the authors, the increased P2 amplitude is associated with the occurrence of positive symptoms and worse functioning, whereas the prolonged latency is associated with the intensification of stereotypical thinking. The duration of visual and spatial training effect on P2 latency was longer than that of the hearing training, which may indicate that hearing discrimination deficits in patients with schizophrenia require more intensive training to gain a more stable change [40–42].

Popov et al. [43] have compared a memory and hearing training with a standard cognitive rehabilitation program. Their research have proven a positive effect on M50 normalization of magnetoencephalographic version of P50 during 4 weeks of study [40–43]; the study was not continued, therefore the duration of the improvement is unknown. Rass et al. [44] have analyzed the influence of visual and hearing rehabilitation exercises with the use of a computer, however, they have not confirmed any significant improvement in hearing P300 directly after the intervention, nor in long-term observation [40–44].

In conclusion, it must be noted that the obtained results convey interesting information associated with brain bioelectrical activity, based on invasive parameters (blood serum) and non-invasive parameters (tests and scales) assumed for this paper. Further research and analyses extension by additional markers shall allow a coherent assessment of the brain functioning, both in terms of quantity (QEEG) and quality (EEG).

It should be stressed that any scientific experiment is subject to certain limitations. In this paper, such limitation is pharmacotherapy. To minimize the risk of errors, the study included only those patients who were in the remission phase, and took only atypical medication (without changes in treatment). It may be assumed that the effect of pharmacotherapy was maintained at a stable level in both examined groups (remission phase), and the obtained improvement in cognitive and social functioning in the group of patients undergoing rehabilitation depended on the applied interventions. The assumption may be confirmed by the studies by Larsson et al. [45], in which the authors indicate the increased BDNF expression as the result of biochemical changes induced by physical exercises, and by Ziemba [46], who claims that systematic strengthening is a condition of a stable level of stimulation, which influences the regeneration and creation of LTP *(long term potentiation)* memory trails [22, 40, 45, 46]. The positive effect of rehabilitation actions has also been confirmed by various authors who claim that anti-psychotic medicines do not improve cognitive functions in patients diagnosed with schizophrenia in a clinically significant manner [46–52], although they are indispensable during the treatment process.

Unfortunately, the pathophysiology of schizophrenia is complex, both in terms of structural [53–55], functional [56, 57], electrophysiological [58–60], neuroendocrine [61–63], immunological [64], and neurochemical disabilities [65–68]. Therefore, it is difficult to distinguish one factor that would obviously influence the improvement in cognitive and social functioning of ill persons. However, the complex diagnostic and therapeutic problems cannot be an obstacle in the search for non-pharmacological forms of therapy.

Positive effects of standard psychiatric rehabilitation, presented in this paper, justify the need for further studies on the techniques of neuromodulation and neurostimulation in patients with schizophrenia [69–72].

Conclusions

The hypothesis assumed in this study confirmed the influence of structured rehabilitation influences on the cognitive and social functioning of people diagnosed with schizophrenia. This is proven by:

1) an increase in the amplitude of SMR, alpha and beta waves in QEEG;
2) an increase in the alpha/beta and SMR/beta frequency ratios,
3) an increase in the brain-derived neurotrophic factor (BDNF),
4) an improvement in cognitive functions and social functioning (CTT-1, CTT-2, d2, AIS, GSES, BCIS),
5) a reduction in negative symptoms (PANSS).

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