

Application of combined drug and music therapy in patients with depression

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Abstract

Depression is a highly prevalent mood disorder, significantly impairing quality of life and associated with increased mortality. Effective interventions usually involve a combination of pharmacological and psychotherapeutic treatments. As individuals respond differently to various therapeutic approaches, a wide range of possible interventions has been devised. However, the potential of music therapy has not been thoroughly researched.

This study aims to investigate the effect of including music therapy in depression treatment. A total of 62 patients, all receiving antidepressant treatment involving escitalopram, were equally divided into an experimental group and a control group. While the control group remained on medication-only treatment, the experimental group additionally participated in a music therapy program consisting of 10 individual sessions, each lasting 50 minutes. The sessions were structured and included both active and receptive components in a predetermined sequence. The active elements included concentration, coordination, short-term memory, and improvisation exercises, which required motor responses to musical and rhythmic prompts. The receptive components were centered on relaxation exercises.

Progress was tracked at three points – at initiation of treatment, on day 14, and at its conclusion on day 90. Each participant was evaluated by a psychiatrist using the Clinical Global Impression–Severity scale and the Global Assessment of Functioning scale and completed the Zung Self-Rating Depression Scale.

Results indicated a positive therapeutic effect in both groups. However, an additional significant improvement in indicators of anxiety, cognitive factors, and social functioning was observed in the group where drug treatment was combined with music therapy.

Keywords

depression, escitalopram, music therapy, social functioning

Introduction

As reported by Santomauro et al. (2021), 193 million people worldwide suffered from depression in 2020,

their number increasing to 246 million following the COVID-19 pandemic. A similar tendency was observed in the prevalence of depression among the population of Central and Eastern Europe, where it increased by 29.4%.

According to data from the World Health Organization (2023), more than 280 million people worldwide suffer from depression, which represents about 3.8% of the overall population. A greater proportion of people with depression are women (5%) compared to men (3%). James et al. (2020) analyzed prevalence, incidence, and years lived with disability for 354 diseases in 195 countries for the period 1990–2019 and found depression to be one of the main factors contributing to deterioration in quality of life and overall functioning.

According to Vittengl et al. (2007), after the first depressive episode there is a risk of recurrence within the following 2 years. Murphy and Byrne (2012) found that depression acquires a chronic course in 30% of patients. The results of the meta-analysis performed by Levkovitz et al. (2011) revealed that only 54% of patients responded to the treatment applied.

A number of researchers have been involved in the search for and development of various treatment strategies, including non-medication therapies such as music therapy, in view of the increase in the number of patients with depression, the risk that the disease may acquire a chronic course, the deterioration of quality of life, and the concomitant family and social dysfunction. The current study pilots a structured music therapy program and explores its effects when administered in conjunction with standard pharmacological treatment.

Materials and methods

The study was carried out as part of the rehabilitation program conducted at the Clinic of Psychiatry at Aleksandrovskaya University General Hospital. Permission was obtained from the hospital's Ethics Commission (No. 66 of 15 June 2022) for conducting a study entitled "Application of individual music therapy in patients with depression".

A total of 69 participants were divided into two groups by matching several criteria, with the aim of ensuring maximum equivalence between them and comparability of their initial conditions. The matching criteria included severity of the disorder (mild or moderate), age, marital status, and educational attainment of the participants. Inclusion requirements for both groups comprised meeting ICD-11 diagnostic criteria for depression (6A70.0; 6A71.0; 6A71.1), not having received music therapy in the past, not participating in any other form of psychotherapy throughout the entire duration of the study, and adherence to pharmacological treatment with escitalopram, as prescribed by the attending psychiatrist. Subjects had to be under 65 years of age and fill out an informed consent form. Excluded from the study were patients with manifestations of depression resulting from alcohol or psychoactive substance abuse; those whose depressive episode was part of the diagnosis of bipolar affective disorder; those whose depressive episode contained psychotic symptoms; or those who presented an increased suicide risk. Seven patients (three

from the experimental group and four from the control group) failed to complete the study, and their data were not processed in the final results. The reasons for their discontinuation were a change of place of living, long-term care for a member of the extended family, and hand trauma that made it difficult to perform exercises with percussion instruments.

Thus, 62 valid datasets were obtained. The control group consisted of 31 individuals, of whom 11 were male and 20 were female, who received medication-only treatment. The experimental group also comprised 31 individuals, of whom five were male and 26 were female, who participated in an individualized music therapy program while also receiving pharmacological treatment. The average age of the patients receiving only antidepressant treatment was 40.39 years (44.36 for men and 38.20 for women); the average age of those receiving the combination treatment was 40.32 years (43.00 for men and 39.81 for women), with no age differences between the two groups. The distribution of the patients according to their education, marital status, and employment is presented in Table 1. No reliable difference was found when comparing the two groups by socio-demographic indices. The greatest was the relative share of single and employed patients in both groups. With regard to education, patients with higher education predominated in the group receiving drug treatment only – 18 (58.10%) – whereas in the group receiving combination therapy, the number of patients with secondary education – 18 (58.10%) – was larger.

Table 1. Socio-demographic data of both groups of patients.

Group/Index		Antidepressant (n = 31)	Antidepressant and music therapy (n = 31)
Education (p = 0.310)	Higher	18 (58.1%)	13 (41.9%)
	Secondary	13 (41.9%)	18 (58.1%)
Marital status (p = 0.310)	Married	9 (29.0%)	7 (22.6%)
	Single	11 (35.5%)	15 (48.4%)
	Divorced	6 (19.4%)	8 (25.8%)
	Widow/er	5 (16.1%)	1 (3.2%)
Employment (p = 0.114)	Employed	23 (74.2%)	16 (51.6%)
	Unemployed	8 (25.8%)	15 (48.4%)

Subsequent analysis showed a larger number of patients with a mild depressive episode in the control group (6A71.0 by ICD-11) – 20 (64.50%) – whereas in the group receiving combined therapy the distribution by severity of the depressive symptoms (mild and moderate) was more uniform. In both groups, the greatest was the relative share of patients with two depressive episodes, as well as of patients negative for family history of mental disorders. Table 2 presents the distribution of patients by diagnosis (ICD-11), number of depressive episodes, and family history of mental disorder.

The pharmacological treatment applied to all patients involved escitalopram, an antidepressant with a good treatment profile. Sleep disturbances were observed in a number of patients from both groups, so hydroxyzine hy-

Table 2. Distribution of patients by diagnosis (ICD-11), number of depressive episodes, and family history.

		Antidepressant (n = 31)	Antidepressant and music therapy (n = 31)
Diagnosis by ICD-11 (p = 0.07)	6A70.0	4 (12.9%)	10 (32.3%)
	6A71.0	20 (64.5%)	11 (35.5%)
	6A71.1	7 (22.6%)	10 (32.3%)
Number of depressive episodes (p = 1.00)	One	9 (29.0%)	10 (32.3%)
	Two	12 (38.7%)	12 (38.7%)
	Three	10 (32.3%)	9 (29.0%)
Family history of mental disorder (p = 0.31)	Positive	5 (16.1%)	10 (32.3%)
	Negative	26 (83.9%)	21 (67.7%)

drochloride had to be included for a period of 14 days at a daily dose of 25 mg. Its effect on depressive symptoms is minimal and clinically insignificant. The daily dose of escitalopram applied in the first 2 weeks was maintained until the end of the third month, during which the patients were followed up. The pharmacological treatment applied (an escitalopram daily dose and hydroxyzine hydrochloride – 25 mg daily in a number of patients in both groups)

Table 3. Pharmacological treatment applied in both groups of patients.

Patient group		Escitalopram (n = 31)	Escitalopram and music therapy (n = 31)
Escitalopram daily dose in mg (p = 0.170)	10 mg	7 (22.6%)	5 (16.1%)
	15 mg	1 (3.8.7%)	6 (19.4%)
	20 mg	23 (74.2%)	20 (64.5%)
Hydroxyzine hydrochloride – 25 mg daily dose for 14 days (p = 0.609)	Used	12 (38.7%)	15 (48.4%)
	Not used	19 (61.3%)	16 (51.6%)

is presented in Table 3.

A psychiatric and self-report assessment was carried out upon initiation of the study, as well as on day 14 and day 90 (when treatment was terminated). The initial evaluation at the beginning of the therapy aimed at establishing each participant's baseline condition. Day 14 was chosen as the next point of measurement because it marked the end of the initial treatment phase. At that time hydroxyzine hydrochloride, which was administered to a limited number of patients, was discontinued. On day 90 the last measurement was performed, marking the conclusion of the medium-term antidepressant treatment course, as by this time it was expected to have reached its maximum therapeutic effect.

The patients completed the Zung Self-Rating Depression Scale (SDS) upon initiation of treatment, on day 14, and on day 90 (when treatment was terminated). Based on their responses, the degree of severity of depressive symptoms was determined as mild (41–47 points), moderate (48–55 points), and severe (over 55 points). SDS consists of 20 statements that have been grouped by Romera (2008), and the resultant four-factor structure helps to investigate depression by breaking it down into affec-

tive, cognitive, anxious, and somatic factors. According to Romera, in this way various depression profiles can be identified, which may be of diagnostic, therapeutic, and prognostic significance.

All participants were assessed by a psychiatrist using the Clinical Global Impression–Severity (CGI-S) scale upon inclusion in the study/initiation of treatment and upon termination of treatment and with the Global Assessment of Functioning (GAF) scale on days 1, 14, and 90 of treatment. In addition, the psychiatrist had to select patients suitable for treatment with escitalopram (antidepressants belonging to different groups have different receptor profiles) at a dose appropriate for each patient's individual needs.

The data were analyzed using statistical software SPSS, version 20.0. The following statistical methods were used to process the data obtained: descriptive statistics – to generalize the results by means of absolute (n) and relative frequencies (%); one-sample Kolmogorov–Smirnov test – to compare prevalence distribution in the quantitative variables (with regard to normal distribution); chi-square test or Fisher's exact test – to study the relation between descriptive data with two or more categories; Mann–Whitney test – to compare the results between two independent groups (the two types of treatment: antidepressant therapy and combined antidepressant and music therapy) when the distribution of the index compared deviated from the norm; Friedman test – to compare more than two connected groups (upon initiation of treatment, on day 14, and day 90 of treatment when patient follow-up was terminated). The accepted level of statistical significance for rejecting null hypotheses was $p < 0.05$.

A piloted music therapy program was developed for the study and administered as part of the rehabilitation program conducted at the Clinic of Psychiatry at Aleksandrovska University General Hospital – Sofia, in patients with various mental disorders (depression, schizophrenia, anxiety disorders, and others) (Ivanova et al. 2021). It consisted of 10 individual sessions, of specific sequence, structure, and content, each lasting 50 minutes. Standard percussion instruments were used, and no musical skills were required of the patients. The therapy followed a predetermined structure of sessions, alternating between musical exercises aimed at stimulating cognitive functions (rhythm, problem-solving, and memory), exercises involving the whole body (coordination, mirror exercises), emotional improvisations, creative tasks, and relaxation techniques. All sessions were carried out with the same music therapist. The 10 individual sessions included active and receptive music therapy in the following sequence:

In the first session the music therapist acquainted the patient with the main principles of music therapy. The patient participated in active music therapy, which included exercises for improving concentration, combined exercises for concentration and movement coordination (arms and legs), and focusing on short-term memory.

- In the second session the patient listened to a relaxing instrumental composition and to nature sounds against background music.
- The third session, like the first, involved exercises for improving concentration and short-term memory (the exercises became more complex with each new session). Similarly to the second session, the patient listened to a relaxing instrumental composition. In the third session the patient interpreted positive and negative emotions, choosing their sequence independently.
- In the fourth session the patient performed exercises of greater complexity, targeting concentration and coordination. With the help of the music therapist, the patient expressed a negative emotion as a somatic sensation, with its body localization; this was followed by an instruction to release the negative emotion and generate a positive emotion. The music therapist helped the patient master techniques for modeling their actual state and emotions with a view to improving self-control. Emotions were improvised in this session.
- During the fifth session the patient continued to improvise various emotions.
- In the sixth, eighth, and tenth sessions relaxation exercises were performed.
- In the seventh and ninth sessions the patient improvised various emotions.

All exercises performed by the patients during the individual sessions, the techniques used in performing them, and the expected results are summarized and presented in Table 4.

Results

All patients self-rated the severity of their depressive symptoms upon initiation of treatment, on day 14, and on day 90 (end of treatment). Table 5 shows the data for both groups and presents the mean, maximum, and minimum values of depression by the Zung scale.

The data summary indicated no significant difference in the mean values on the Zung scale between the two groups of patients – the ones receiving antidepressant treatment only (46.03 ± 2.44 points) and those receiving combination therapy (45.03 ± 2.75 points). The initial tendency toward a difference in the self-rating of depressive symptoms between the two groups was preserved at the end of the second week. At the end of the third month of treatment, the mean values on the Zung scale were 40.65 ± 1.80 points and 38.52 ± 1.75 points in the patients on antidepressant therapy and in those on combination therapy, respectively, which revealed a significant difference ($p < 0.001$).

Table 4. Music therapy program: exercises, techniques, and expected results.

Individual exercises and the technique to perform them.	Results
Rhythm exercises with a percussion instrument; legs can also be included	
The patient uses a percussion instrument (drum), drumming directly on it with fingers/palm. With each new session the exercises become more complex, with the patient's legs contributing to the rhythm. Various rhythm combinations are used in the separate sessions.	The rhythm exercises are directed toward improving concentration and short-term memory, achieved by learning and reproducing short rhythm models.
Rhythm exercises, including upgrading with short solo answers	
The therapist determines the musical models and allows the patient to make a free improvisation. Through eye contact the therapist conveys the model and responds to the solo answer of the patient.	In a protected environment the patient is given the opportunity to make a solo performance in response while receiving active support from the therapist.
Logic exercises	
The therapist performs musical models with percussion instruments that gradually become more complex in the course of sessions, and the patient performs them.	Improvement of short-term memory
Exercises for active maintenance of eye contact	
The therapist and the patient use eye contact to convey short sound signals to each other.	Improvement of concentration and stimulation of non-verbal communication
Mirror exercises	
These exercises combine movement and sound. One participant, the Performer, follows what the other participant, the Leader, does and simultaneously performs the opposite. In the course of the exercise, the therapist and patient exchange roles – first one is the leader and the other the performer, then vice versa.	Improvement of concentration
Creative exercises	
The patient enacts emotions by choosing either a positive or a negative one, along with the type of instrument that will facilitate this expression.	The patient is stimulated to communicate and share emotions in a protected environment.
Improvisation	
The patient chooses an instrument, allowing the therapist to determine the timbre, pitch, and intensity of the tone. Improvisation may be accompanied by movement of the body or part of it.	Helps the patient make independent decisions.
Exercises for emotional self-control	
The patient uses sound as a means of releasing negative emotions and subsequently performs improvisations that create a relaxing effect.	Helps the patient cope with negative experiences.
Relaxation exercises	
The patient combines movement and the production of sounds of the appropriate timbre. Breathing techniques are taught, and the patient practices them.	The patient learns relaxation techniques.

Table 5. Dynamics of depressive symptoms during the study period for both groups of patients.

	Patient group	Mean \pm SD	Min. value	Max. value
Upon initiation of treatment ($p = 0.116$)	Escitalopram ($n = 31$)	46.03 \pm 2.44	41.00	51.00
	Escitalopram and music therapy ($N = 31$)	45.03 \pm 2.75	41.00	50.00
At the end of the second week of treatment ($p = 0.049$)	Escitalopram ($n = 31$)	40.90 \pm 1.51	38.00	44.00
	Escitalopram and music therapy ($N=31$)	39.00 \pm 2.09	33.00	43.00
At the end of the third month of treatment ($p < 0.001$)	Escitalopram ($n = 31$)	40.65 \pm 1.80	37.00	44.00
	Escitalopram and music therapy ($n = 31$)	38.52 \pm 1.75	36.00	44.00

In addition to the depression level as measured by the Zung scale, an additional analysis was performed on the breakdown of the cumulative indicator into four component factors, which were compared between the groups for the study period. The results are presented in Fig. 1.

At the end of treatment, the comparison between the two groups revealed a significant difference in two of the factors – anxiety and cognitive function ($p < 0.001$) – in the patients receiving the combination treatment. The reduction in anxiety and improvement in cognitive function most likely influenced the way in which they self-rated their depressive symptoms.

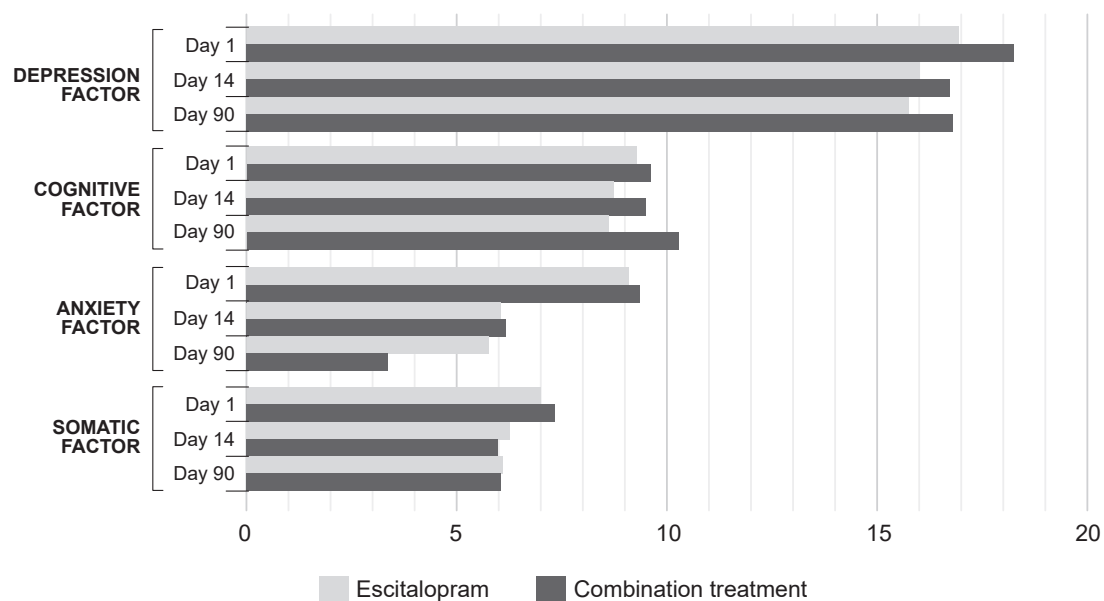
A psychiatrist assessed the patients upon initiation of treatment, on day 14, and at the end of treatment using CGI-S. The results are shown in Table 6.

The depressive symptoms were assessed in each participant in the study using the Zung Self-Rating Depression Scale, as well as by a psychiatrist using the CGI-S scale. Based on the data presented in Table 7, it may be concluded

that in both groups the prevalent number of patients manifested mild depression: 24 patients (77.40%) who received antidepressant treatment and 21 patients (67.70%) who received combination treatment. The fact that the greater part of the patients had mild depressive symptoms should be taken into consideration when interpreting the results.

The relative share of patients on escitalopram treatment at a daily dose of 20 mg predominated, with 23 patients (74.20%) receiving antidepressant treatment and 20 patients (64.50%) receiving combination treatment. Sleep disturbances required the administration of hydroxyzine hydrochloride at a daily dose of 25 mg for 14 days in 12 patients (38.70%) receiving antidepressant therapy and in 15 patients (48.40%) receiving combination therapy. After the 14-day period hydroxyzine hydrochloride was discontinued.

The social functioning (GAF) of all patients was assessed by a psychiatrist upon inclusion in the study and at the end of the third month of treatment. The results are presented in Table 8.

**Figure 1.** Comparison between the two groups of patients using the Zung scale four-factor structure.**Table 6.** Comparison between the two groups in assessing depression on the CGI-S scale.

		Escitalopram ($n = 31$)	Escitalopram and music therapy ($n = 31$)
CGI-S upon initiation of treatment ($p = 0.570$)	Mildly depressed	24 (77.4%)	21 (67.7%)
	Moderately depressed	7 (22.6%)	10 (32.3%)
CGI-S at the end of second week of treatment ($p = 0.384$)	Bordering on depression	6 (19.4%)	10 (32.3%)
	Mildly depressed	25 (80.6%)	21 (67.7%)
CGI-S at the end of third month of treatment	Within norm	31 (100.0%)	31 (100.0%)

Table 7. Comparison of social functioning in both groups of patients upon initiation and termination of treatment.

Patient group\Index	Mean \pm SD	Min. value	Max. value
GAF upon initiation of treatment ($p = 0.005$)			
Escitalopram ($n = 31$)	52.81 \pm 7.41	41.00	63.00
Escitalopram and music therapy ($n = 31$)	46.29 \pm 7.81	31.00	61.00
GAF upon discontinuation of treatment ($p < 0.001$)			
Escitalopram ($n = 31$)	92.06 \pm 1.88	90.00	97.00
Escitalopram and music therapy ($n = 31$)	97.00 \pm 2.47	91.00	100.00

Table 8. Brain structures, escitalopram receptor profile, functional importance, therapeutic effect of escitalopram administration, influence of music therapy, and literature source.

Brain structure	Escitalopram receptor profile	Functional importance	Escitalopram effect	Influence of music therapy (active and receptive)	Source
PFC	High density of SERT, 5-HT _{1A} and 5-HT _{2A} receptors	Increases serotonergic activity, which improves cognitive functions, emotion control, and executive functions	The increase in serotonin levels results in improving mood and cognitive functions	Active: improves motor and cognitive functions Receptive: influences emotion regulation and acts as a relaxant	Thoma et al. 2013; Stahl 2013; Takano et al. 2006; Koelsch 2014; Harmer et al. 2008; Flaisch et al. 2021
Amygdala	High density of SERT, 5-HT _{2A} receptors	Reduces anxiety by modulating emotional reactions	Results in reduction of anxiety and fear reactivity	Active: assists in expressing emotions through music and results in stress reduction Receptive: reduces stress and anxiety through listening to music	Meyer et al. 2004; Koelsch et al. 2010; Thoma et al. 2013; Stahl 2013; Koelsch 2014; Altenmüller and Schlaug 2015
Hippo-campus	SERT and 5-HT _{1A} receptors	Memory, learning, and stress regulation	The increase in 5-HT results in improvement of memory and neurogenesis	Music has a stimulating impact on the hippocampus – it improves cognitive processes and emotional state	Invernizzi et al. 1996; Koelsch et al. 2010; Flaisch et al. 2021
mPFC	SERT and 5-HT _{1A} receptors	Regulates social behavior and self-reflection	Escitalopram modulates the default mode network (DMN) and emotional coherence	Music therapy increases DMN functional connectivity	Takano et al. 2006; Koelsch 2014; Harmer et al. 2008; Saarikallio et al. 2020; Flaisch et al. 2021
Striatum	SERT, dopamine D ₂ receptors	Motivation, reward system, and motor control	Escitalopram acts predominantly through serotonin mechanisms	Active music therapy results in striatal activation, which increases motivation and improves mood	Takano et al. 2006; Thoma et al. 2013

The result of the GAF assessment of social functioning was 52.81 ± 7.41 in the patients receiving antidepressant treatment and 46.29 ± 7.81 in the patients receiving combination treatment – a significant difference ($p = 0.005$) was observed between the two groups. In the course of treatment, change was observed in both groups, with significant improvement in social functioning in the patients receiving combination therapy ($p < 0.001$).

Discussion

Women predominated in the study – 46 (75.41%) compared to men – 16 (26.23%). This difference is likely to have influenced the results, but it also reflects the fact that depression occurs more frequently in women. Kornstein et al. (2000, 2002) reported that anxiety is more severe in women with depression and is reduced in the course of depression treatment. These authors also stated that depression and anxiety negatively impact cognitive processes, and they regard depression treatment combined with music therapy as an alternative modality or a way of expressing the emotional state of patients.

The application of four-facet analysis in the studied patient group enables the identification of potential differences in depressive profiles, based on the distribution of affective symptoms, cognitive deficits, anxiety manifes-

tations, and somatic complaints. In the present study, this analytical approach was employed to differentiate depressive subtypes that may influence both the course of the disorder and the efficacy of the combination treatment. The findings demonstrate a significant reduction in anxiety-related symptoms, as well as a marked improvement in cognitive functioning among patients who received the combined therapeutic intervention (Fig. 1). For greater objectivity in determining the potential impact of combining pharmacological treatment and music therapy, all participants in the study received drug treatment involving the same antidepressant.

Degli et al. (2016) analyzed the data of a randomized study of patients with different mental disorders, including depression, who received combination drug and music therapy, in which the therapeutic effect of antipsychotics was achieved at a lower daily dose compared to the control group. The same researchers found a similar tendency in antidepressants, although statistical significance was not observed.

In the present pilot study, the greatest relative share of patients from both groups experienced therapeutic effects at daily administration of 20 mg escitalopram: 23 patients (74.20%) receiving antidepressant treatment and 20 patients (64.50%) receiving combination treatment. Further studies on larger groups of patients receiving combination treatment are required to establish the potential positive therapeutic effects.

Escitalopram is an antidepressant classified as a selective serotonin (5-HT) reuptake inhibitor (SSRI) and acts by improving serotonergic neurotransmission. The effect of the drug is associated with a serotonin transporter (SERT) protein and inhibition of serotonin reuptake. Escitalopram has high selectivity and minimal influence on other neurotransmitter systems. A number of researchers (Stahl 2013; Cipriani et al. 2018; Harmer et al. 2008; Koelsch 2014) assume that the combination of escitalopram and music therapy (active and receptive) probably leads to a synergistic effect – therapeutic effects can be achieved at a lower daily dose of the medication, which in turn reduces the risk of side effects. These authors consider that escitalopram produces its therapeutic effect by interacting with certain brain structures: the prefrontal cortex (PFC) – improves cognitive control and emotion regulation; the amygdala – reduces anxiety; the hippocampus – influences memory and emotion regulation; the striatum – influences motivation and motor activity; the medial prefrontal cortex (mPFC) – participates in the regulation of social behavior. Table 8 presents the brain structures, the escitalopram receptor profile, the impact of music therapy, and the literature sources.

Särkämö et al. (2016) assumed that music therapy created conditions for building a “broad bilateral network” involving the temporal, frontal, parietal, cerebral, and limbic/paralimbic brain structures associated with auditory perception, language, syntax and semantic processing, attention and working memory, motor functions, and emotions. These researchers looked for a crossing point between neuroscience and music therapy with a view to finding the presumed neuronal mechanisms underlying the therapeutic effect of music therapy and its inclusion as part of rehabilitation programs. A number of researchers (Thayer and Lane 2000; Blood et al. 2001; Salimpoor et al. 2011; Trost et al. 2012) suggested the presence of shared neuronal networks involved in the regulation of emotions and cognitive processes, with the participation of the autonomic nervous system (ANS) – the recorded alterations in heart rate, breathing, body temperature, and other parameters give grounds to assume the presence of a model of neurovisceral integration. Sihvonen et al. (2017) found that music influenced the cardiovascular and endocrine systems and decreased serum cortisol levels. They share the opinion that inhibition of the sympathetic nervous system and activation of the parasympathetic nervous system also assist in restoring patients’ cognitive functions. Because of the diversity in the clinical manifestation of depression, some researchers (Määttä et al. 2019; Xiao et al. 2023) differentiate between various subtypes based on the activity and reactivity of the parasympathetic ANS, which could help in developing treatment strategies.

The music therapy administered to our patients with depression included both active and receptive types, with a duration of 10 sessions. The music therapist developed complex exercises that corresponded fully to the actual state of the patient. The active exercises predominated in the music therapy administered and were directed at im-

proving the emotional, cognitive, motor, and communication skills of the patients. The exercises, how to perform them, and the expected results of the individual sessions are described in detail in Table 4; they targeted above all the function of the frontal lobe of the brain.

Improvisation occupied a considerable part of the treatment sessions, since the patient was in a situation in which they had to make relatively quick decisions regarding timbre, rhythm, intensity of the sound, and other musical aspects by means of the instrument they had chosen. The positive effects of clinical improvisation consisted in improving the patient’s ability to make independent decisions.

According to Stern (2010), the power of improvisation within the treatment context lies in the creation of a space in which the patient can find symbolic solutions to various problems. When the patient improvises, their attention is focused on the “here and now” – the purpose is to mobilize resources for problem-solving, since prolonged disease frequently results in lack of self-confidence. The meetings between patient and music therapist underlie the creation of a therapeutic relationship in which they share subjective experiences within the treatment process.

Various topics were discussed in our course of music therapy, to which patients arrived burdened with negative emotional experiences, and improvisation helped their therapeutic release. The music therapist managed the stress level and its duration during the session. Clinical improvisation provided an opportunity to share emotional experiences, which could be analyzed and interpreted afterward. The improvisations were topically related to actual feelings and experiences, and sharing them in a protected environment was encouraged. Musical improvisation helped and stimulated the patients to verbalize their experiences more – an activity they may find difficult under the influence of depression.

The music therapy sessions of the studied patients were carried out in a structured therapeutic frame. Music therapy helped improve patient cooperation by establishing the “dose,” defined as the number of sessions. The 10 sessions included elements of both receptive and active music therapy that all patients listened to and performed. All patients received the same “music therapy dose” and the same antidepressant.

Based on their research into the dynamics of depressive symptoms, Algoodkar et al. (2019) reported that a better response to treatment was observed when combining an antidepressant with music therapy twice a week for a period of 2 months.

Erkkilä et al. (2011) pointed out that apart from the significant reduction in depressive symptoms, social functioning and compliance were improved in patients receiving drug treatment and individual music therapy.

Analyzing 28 studies involving 1810 participants who had received music therapy, Leubner et al. (2017) reported that 26 of these studies showed improvement in depressive symptoms. Music therapy was more effective in older patients compared to younger ones. Group sessions yielded better results than individual ones. After receiving music

therapy, patients demonstrated a significant improvement in self-confidence and self-esteem, as well as increased motivation to participate in other treatment modalities and a reduction in anxiety.

A number of researchers (Silverman 2011; Bradt et al. 2013a,b; Bruscia 2014) are of the opinion that individual music therapy has advantages in creating a purposeful, flexible, and confidential treatment environment and may be more effective compared to group therapy, which also has advantages with regard to social interaction and building support in the community.

The program for music therapy used in the present study was developed and carried out by our music therapist at the Clinic of Psychiatry as an integrated and personalized sequence of 10 sessions. The participation of one and the same therapist in this process offers the advantage of a complete and coordinated approach – an opinion shared by other authors as well (Bradt et al. 2013a,b; Leubner and Hinterberger 2017; Magee et al. 2013). The music therapist:

- adapted the sessions according to the needs and reactions of each patient;
- helped establish an improved therapeutic relationship – the constant contact with the same therapist increased the patient's trust and sense of safety;
- provided a balance between active and receptive music therapy and a smooth transition between them based on the patient's condition and progress;
- effectively monitored the patient's dynamics so that the treatment strategy could be adjusted and maximum results achieved within the relatively short period of 10 sessions;
- assisted in the patient's adaptation.

As far as the “dose” of music therapy is concerned, Erkkilä et al. (2011) believe that individual music therapy (20 sessions, 60 min each) results in significant reduction of depressive symptoms; others, like Leubner and Hinterberger (2017), recommend shorter to medium programs (4–12 sessions) as having the greatest therapeutic effect and group therapy (12 sessions, 45 min each) as leading to improvement of mood and social engagement, especially in older people (Chan et al. 2012).

Conclusion

The application of combination treatment involving an antidepressant and both active and receptive music therapy had a favorable effect on depressive symptoms, with a reduction in anxiety and improvement of cognitive functions. The application of a combination approach led to improved treatment results, which was probably due to the synergistic effect of the antidepressant/music therapy combination; on the other hand, it offered the patients an opportunity to express, become aware of, and release their negative emotions. Music therapy improved the patients' adaptivity by taking into account their actual state and by

applying both active and receptive approaches within the treatment sessions. The combination therapy improved the patients' motivation and engagement in the treatment process.

The present study investigated the medium-term effect of applying music therapy to the treatment of depression. The combination treatment involving music therapy provides an opportunity to develop a set of exercises that influence emotional, cognitive, motor, and communicative skills, while considering the individual challenges of each patient.

The proposed program can be considered an innovative intervention tailored to the needs of patients with depression. It can be used in its entirety or modified as part of rehabilitation programs for patients with various mental disorders. The outcomes of the current study suggest that this individual music therapy significantly contributes to the overall treatment and recovery of patients, especially when applied in conjunction with medication therapy.

Limitations and future research

This is a pilot study, and the results obtained must be interpreted with respect to the following restrictions. The comparatively small number of participants reduced the statistical significance of the findings, as well as their generalizability to a wider population. It also prevented complete randomization of the sample and necessitated the use of matching criteria based on several clinical indicators to ensure the equivalence of the experimental and control groups. The lack of prolonged observation extending beyond the 90-day period of treatment does not allow for an assessment of the long-term effect of the combined treatment. The methods used to assess depression were focused on monitoring the dynamics of depressive symptoms, whereas follow-up of social functioning may require a longer period – a medium-term follow-up from 1 to 4 months after the conclusion of the therapy. The imposed severity-level requirement of mild to moderate depression and the exclusion of patients with comorbidities and suicide risk increased the internal validity of the study while decreasing the external validity, as the findings could not be directly applied to all patients suffering from depression, in particular to those with severe depression and those exhibiting psychotic symptoms. Additional limitations include the narrow age range of the participants, the predominance of women over men, the selection of an antidepressant agent appropriate for all patients studied, and the assessment of depressive symptoms by the patients themselves.

Future studies should focus on developing and applying standardized programs for active and receptive music therapy to facilitate the comparison of results obtained in different studies, as well as on long-term investigations and comparisons of individual and group music therapy settings.

Multidisciplinary studies are needed, as well as long-term follow-up of a larger number of patients with depression, given the diversity and clinical manifestations of

the depression spectrum. Identifying the nuances of depression and finding biomarkers would help develop new strategies in the treatment of this mental disorder.

Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that experiments on humans or human tissues were performed for the present study.

Informed consent from the humans, donors or donors' representatives: Currently kept by the authors of the study.

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- ### Data availability
- All of the data that support the findings of this study are available in the main text or Supplementary Information.
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