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Music Therapy and Pharmacotherapy as a Combination Treatment: A Case of Periodic Depression in Comorbidity With Subthreshold Autism

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ABSTRACT

Subthreshold Autism Spectrum Disorder (ASD) can complicate depression treatment as ASD may hinder treatment benefits. In this case, a patient in treatment for recurring depression with traits of ASD showed symptom reduction, improved relational functioning, and emotion regulation skills by combining pharmacotherapy and music therapy.

1 | Introduction

Major Depressive Disorder (MDD) is a mood disorder marked by sadness, low energy, diminished motivation, sleep changes, feelings of guilt, low self-esteem, suicidal thoughts, and cognitive issues.

MDD is a significant source of personal suffering and economic burden, with prevalence rates ranging from 2% to 21%, varying by region. It is often associated with child abuse, intimate partner violence, and comorbidities, with higher rates in women and those lacking strong social networks [1]. In the U.S., the annual cost of medication-treated MDD is $92.7 billion, with nearly half attributed to treatment-resistant depression (TRD) [2]. Many individuals with MDD do not respond to treatment, and TRD can be exacerbated by the presence of other mental disorders, such as Autism.

In 2019, MDD was the leading cause of Disability-adjusted Life Years (DALYs) among young adults in Denmark and other high and medium Socio-Demographic Index (SDI) countries [3]. MDD can be classified as mild, moderate, or severe based on symptoms and their intensity. Treatment typically involves psychotherapy or a combination of psychotherapy and medication [4]. Unfortunately, only 30% of patients achieve remission with first-line antidepressants, partly due to comorbid conditions [5, 6].

Autism Spectrum Disorder (ASD), characterized by social communication challenges and limited interests, may impact the effectiveness of MDD treatments. With a prevalence of 1.9% [7], symptoms of ASD—such as concentration difficulties, muted facial expressions, social withdrawal, and sleep issues—often overlap with those of depression. Individuals with ASD have a four-fold higher risk of experiencing significant depression. In particular, the pooled lifetime and current prevalence was reported to be 14.4% (95% CI 10.3–19.8) and 12.3% (95% CI 9.7–15.5), respectively [8]. Of note, symptoms of depression can be found early in individuals with ASD, also in pre-teenage periods. This may be related to the social difficulties of these individuals, further complicated by their difficulties in interpreting others' and their own emotions [9]. Such difficulties may also be responsible for a higher mortality rate in individuals with ASD compared to the general population [10]. Subthreshold ASD can further complicate MDD treatment, as its traits may hinder the benefits of psychotherapy [11].

For those with ASD, depressive episodes are often triggered by social stress or relationship failures, where pharmacological treatment may only address symptoms rather than underlying issues. Additionally, individuals with mild ASD and normal cognitive abilities frequently experience delayed diagnoses, resulting in years of ineffective depression treatment before recognizing subthreshold ASD. This population is also more prone to conditions such as sleep disturbances, gastrointestinal issues, ADHD, anxiety, obesity, eating disorders, and disruptive behaviors [12]. Comorbid anxiety and depression are particularly prevalent among individuals with low-functioning ASD compared to those with high-functioning autism [13]. Quite interestingly, males with ADD were reported to be more at risk of experiencing depression than their female counterparts. This difference becomes less evident after the age of 24 years [9]. Conflicting reports are also found [14].

2 | Case Report

2.1 | Patient Information

S is a 44-year-old man undergoing treatment for depression at Aalborg University Hospital's Outpatient Unit. He works in IT but is currently on sick leave due to MDD. S lives in an apartment and spends time with his adolescent son, who has ASD, while maintaining a good relationship with his ex-wife.

S's first depressive episode occurred at 20 during his university studies in IT. He began treatment with citalopram (40 mg/day) in 2002, which he used intermittently for about 7 years.

In 2009, he experienced a severe episode with suicidal thoughts and resumed citalopram treatment, coinciding with his marriage. In February 2010, he sought help again, reporting sadness, low energy, and suicidal thoughts, leading to a combination treatment of citalopram and mirtazapine until April 2011.

S was hospitalized in March 2012 for severe suicidal thoughts and remained until May, receiving treatment with venlafaxine, duloxetine, mirtazapine, and citalopram. In November 2012, he attempted suicide by overdosing on psychotropic drugs while his wife was pregnant, feeling overwhelmed by the situation.

S continued outpatient treatment until 2015, when he was diagnosed with dysthymia. He was hospitalized again in February 2022 for depressive symptoms and has been in outpatient treatment since his discharge in March 2022.

2.2 | Family History

S was born in Denmark to a mother, a father, and an older brother. His father worked abroad for extended periods and was emotionally distant. The mother provided structure for the children but lacked emotional presence or genuine interest in S's feelings.

S describes his childhood and adolescence as safe and normal, though he experienced an inhibition to engage in social activities, which led to isolation and feelings of loneliness. There are no signs of psychological or physical trauma.

He had a challenging relationship with his older brother, who bullied him and dominated their interactions, leaving unresolved dissonance into adulthood.

S's uncle exhibited depressive symptoms, but little is known about his mental health history. The family has no records of bipolar disorder, schizophrenia, substance abuse, or suicidal behavior.

S's son and nephew have been diagnosed with ASD.

2.3 | Clinical Findings

Figure 1 reports S's clinical history.

S received treatment for depression from March 2022 to December 2023 after being discharged from the inpatient unit. At his first outpatient appointment, he was diagnosed with recurrent moderate depression. Currently on sick leave from his IT job, S lives alone but has regular contact with his son, a supportive family, and a girlfriend with whom he lives apart. He is prescribed lamotrigine (100 mg/day) and wishes to start psychotherapy with a familiar psychologist. Instead, he accepts music therapy, with psychotherapy on hold and infrequent follow-up consultations.

During outpatient treatment, S experiences fluctuations in sadness and periods without depressive symptoms, but recovery is slow, marked by progress and setbacks. He is consistent in attending appointments and is seen as gentle and trustworthy.

Various pharmacological treatments targeting his sadness and fatigue have been attempted, including citalopram, lamotrigine, aripiprazole, modafinil, quetiapine, pregabalin, escitalopram, and nortriptyline. Most medications have been poorly tolerated due to side effects or a lack of efficacy. The most effective combination for S has been citalopram (10 mg/day) and nortriptyline (100 mg/day), which he tolerates despite experiencing anticholinergic side effects.

From June 2022 to November 2023, S attended 45 individual music therapy sessions at Aalborg University Hospital.

S was tested for ASD during the period of treatment. It was not possible to give a full diagnosis of ASD since "[the test] shows no signs of deviant social interaction or qualitatively deviant communication. There is also no narrowed repetitive and stereotyped behavioral interest and activity pattern. There are some accentuated personality traits, difficulties with affect regulation, which are expressed in a rigidity and some rigid systems, which S describes as giving him peace."

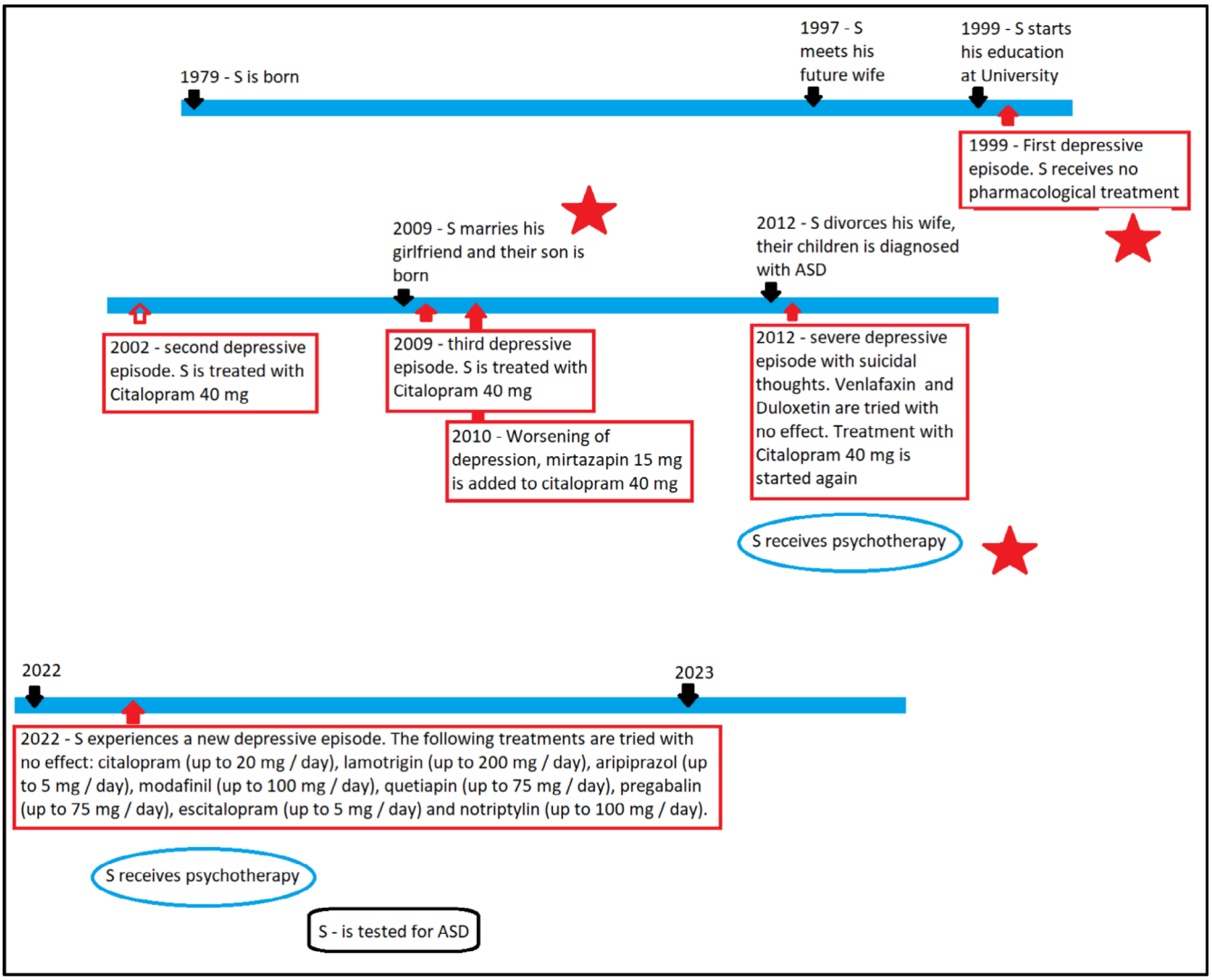

FIGURE 1 | S's clinical history is plotted together with his major life events. The three blue lines indicate time flow. They are best interpreted as a unique line that has been divided into three lines. Recent events are described in a lower position than the older ones. The red stars indicate relevant events.

TABLE 1 | Symptoms of ASD than were found in S's clinical history and presentation.

Symptoms	Asperger's	High functioning Autism	Autism	S
Impairment in social communication	+	++	+++	+/−
Impairment in social relationships	+	++	+++	+
Restricted pattern of interests	+	++	++	+
Eccentric manners	+	++	+++	+
Cognitive delay	−	+	++	−
IQ < 70	−	−	+	−
School learning disabilities	−	+	++	−
Anxiety and Depressive comorbidity	++	+	+	++
ADHD comorbidity	+	+++	++	−

Note: The table is built based on the following resources in literatures [15–17]. The shadowed boxes indicate symptoms that can be traced down in S's history.

Table 1 reports symptoms of ASD that were found in S's clinical history and presentation and supports the notion of a subthreshold ASD.

2.4 | Music Therapy

Music therapy is a treatment modality in psychiatry. At Aalborg University Hospital, music therapists have been part of psychiatry since the 1990s. Music therapy covers a range of methods, from listening to music to playing or singing songs or a free improvisation. The structure of sessions and the degree of verbalization may vary.

"Music therapy is a reflexive process wherein the therapist helps the client to optimize the client's health using various facets of music therapy experience and the relationship formed through them as the impetus for change" [14].

Music therapy has been found to be effective in the short-term treatment of depression [18]. Longer-term outcomes need further investigation . A systematic review investigating the effects of music therapy for depression, ASD, dementia, insomnia, and schizophrenia concludes that music therapy helps improve physical and psycho-social health across diagnoses [19].

Clinical guidelines point to treating depression by combining medication with psychiatric counseling or psychotherapy. Still, for some patients, verbal processing may be insufficient. In music therapy, music is an alternative expressive modality helping the individual get in touch with emotions. The mechanisms of action in music therapy for depression are multiple. Music-based affect self-regulation enhances modulation of emotional states through music [20–22]. Research points to components of emotional processing, including expression, awareness, and pain, as integral working mechanisms for music-based emotional processing predicting outcomes in depression treatment [21]. In addition, music's ability to modulate emotion and mood in individuals with ASD is well known and reported [15].

Music, both in the form of passive listening and active playing, has been shown to activate areas of the brain involved in cognitive, sensorimotor, and perception-action mediation through increasing the oscillation synchrony between these various cortical areas and thereby promoting heightened sensory integration [16].

The patient was referred to music therapy, and the referral drew on patient reports of using music as a coping strategy since childhood for emotional outlet and support. S. had no musical skills but showed initial motivation for music therapy. The patient attended 1-hour sessions of individual music therapy with a certified music therapist for a period of 18 months. The method was psychodynamic-oriented music psychotherapy.

Two randomized controlled trials have reported positive results from using this method in individual depression treatment [17, 23].

In this case, music therapy included music listening to song recordings from the patients' own playlists and free improvisations on drums and piano.

S. had always been quiet and somewhat invisible to parents and classmates. He had never spoken up, not even when bullied. S. investigated suppressed emotions of anger towards his older brother. S. was very composed, polite, and in control, and expressing aggression was associated with fear of losing control. The childhood conflicts between S. and his brother may have led to the suppression of emotions in adult life, and this could be key to emotional difficulties and recurring depression. The expression of aggression was prepared and initiated in agreement. The emotion outlet was reinforced by a hard rock music piece with aggressive lyrics from the patients' playlist played loudly. S. played hard on the drum set, supported by the music therapist playing on the bass drum. The hard rock play-along supported S. in expressing anger and frustration in a musical non-destructive setting without losing control. This experience was effective in gaining contact with difficult emotions, and it was provoking bodily reactions of trembling and relief. In this situation, S. showed the ability to express suppressed emotions of anger and frustration. S. did not experience this as a core to his emotional problems.

S. often came into music therapy crying, overwhelmed by feelings of sadness and hopelessness. Encouraged by the mt., free improvisations in duet on two pianos were initiated. S. started playing single notes with one finger softly, with significant emotional depth. The mt. mirrored the expression while playing simultaneously alike. S. stated that the music expressed feelings of love, tenderness, and sadness. The playing demonstrated expressiveness of emotional intensity, depth, and clarity. In relation to these more acceptable emotions, no hesitation or suppression came across. S. demonstrated easy access to inner states, including a range of intense emotions clearly expressed musically. Emotions were expressed in forms best described as pure. The music therapist categorized the musical expression typical for emotion expression in ASD. Based on this assessment, the music therapist recommended testing for ASD. S. stated that he felt these emotions strongly on an everyday basis and, in some cases, it was so overwhelming that it would cause a mental breakdown and he would stay in bed for days.

The aim for the therapy was to explore and familiarize with musical expressions of intense emotions by playing together with the music therapist and to investigate possible options of affective mobility, for example by playing differently, changing the dynamics and the character of the music moving from one musical expression to another. The patient explored affective mobility while playing music on the piano in duet with the music therapist. Initially, S. was encouraged to register whatever affective content arose while playing and to "defuse" the affective state by moving or changing the music by introducing a new musical ambiance or simply playing differently. Defusing was named "skating" in verbalization, using the metaphor to visualize detachment from intense emotions. Hereby, S. explored changing his way of playing from intense emotional to less intense/more superficial musical expressions. In the following months, S. improvised expanding the range of emotions from tenderness, love, and sorrow to chaos, anger, and frustration. The mt. shared and

contained the emotions expressed musically. The music improvisations and visualizations encouraged S. to reflect upon his situation. S. spontaneously visualized while playing, he saw an inner film which he explained after playing. S. experienced successes initiating musical change from one type of emotional expression to another. He succeeded in “skating”, that is, playing superficially, touching upon a musical-emotional theme without going into emotional depth, but this was difficult, sometimes impossible.

During this period, S. was encouraged to identify potential “emotion-loaded” situations in his everyday life, for example in relation to his son. S. responded positively to practicing “skating” that is, emotional mobility in real life as this had been rehearsed in therapy. He expressed faith in the process of working with regulating emotions to potentially overcome situations associated with substantial stress and chaos. The ability to gain control through conscious emotion regulation empowered him to feel in control.

It also promoted an increased awareness of potential emotion-loaded situations, which he could prepare for or avoid. Sometimes, regulation was impossible due to rigidity.

Experimental musical investigations of affective mobility were tested both with S. as a leader, taking initiative, and as a follower. S. showed high sensitivity and ability to both lead and follow, indicating a high level of interpersonal relational flexibility.

The therapeutic process evolving in musical improvisation developed from symbiotic contact, where the patient was unable to separate his sounds from the sounds by the music therapist. Later, there was a clear distinction of two instruments playing together. In developmental psychology, the process from symbiosis to individuation is characteristic for the early mother–child development, and a similar process took place between the patient and the music therapist in the musical interaction.

In the later sessions, S. gained a more comprehensive understanding of his emotional sensitivity, which he recognized as neuroatypical.

By the end of the therapy, S. felt that music therapy had helped him regulate his emotions and provided coping strategies. In addition, S. accepted the emotional sensitivity and rigidity as a part of his personality.

3 | Discussion

This case study focuses on S, who has experienced multiple depressive episodes and has tried various pharmacological and psychotherapeutic treatments. S's treatment eventually included a combination of music therapy and antidepressants. While medication provided symptom relief, music therapy helped him develop strategies for managing low energy and suicidal thoughts, offering a safe space to explore and process emotions [23].

Recent findings suggest that ASD is linked to atypical brain information processing. Music therapy may have enabled S. to effectively integrate his emotions through creative expression, as it allowed him to navigate feelings that previously caused chaos [24]. This nonverbal approach facilitated emotion regulation in a supportive environment.

Neurobiologically, musical improvisation has been shown to influence brain activity, particularly enhancing areas associated with creativity and cognitive flexibility, which are often challenging for individuals with Autism [24, 25]. Though S did not receive an ASD diagnosis, he exhibited features consistent with the condition and demonstrated improved emotional regulation skills through music therapy, using compensatory strategies to maintain normal relational functioning.

Future research comprising patients affected by depression and sub-threshold ASD investigating the effects of music (listening, playing, improvising) on the brain and psyche in relation to emotional processing may illuminate the mechanisms of action in music therapy.

For perspectives on the effects of music on brain activity, the reader may follow research from the Center for Music in the Brain, Aarhus University Hospital (DK) and the publications on music therapy, neuroscience, and social cognition by Stefan Koelsch [16, 26, 27].

A single case study does not allow for generalizations. Despite this limitation, this study provides insights into a successful treatment trajectory that may inspire clinicians and researchers to investigate the effects of combining pharmacotherapy and music therapy in a clinical trial.

4 | Conclusion

In this case study, we demonstrated the effects of depression treatment combining pharmacotherapy and music therapy. Special clinical attention to subthreshold autism is required when treating recurrent depression.

In an interdisciplinary effort, we were able to support the patient's treatment needs despite the absence of guidelines for the clinical care of patients with these comorbidities. This case showed the beneficial effects of combined pharmacotherapy and music therapy in outpatient treatment for depression.

The pharmacological treatment included citalopram (10 mg/day) and nortriptyline (100 mg/day). Music therapy replaced traditional psychotherapy as music supported the modulation of emotions.

Recognition of sub-threshold autism in the treatment trajectory may serve to optimize treatment and improve satisfaction for clinicians and patients.

5 | Patient Perspective

S. reported satisfaction with the treatment in the outpatient unit and expressed gratitude for the treatment. He was initially motivated for music therapy and started therapy with a positive attitude.

S was informed of the intention to communicate his case in writing, and he approved of this, while he had no wish to participate in the writing. He expressed a wish to read the final manuscript.

Author Contributions

Helle Nystrup Lund: conceptualization, investigation, methodology, project administration. **Antonio Drago:** conceptualization, investigation, methodology, project administration, supervision, validation.

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Ethics Statement

Ethical review and approval were not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the individual(s) and minor(s)' legal guardian/next of kin for the publication of any potentially identifiable images or data included in this article.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The raw data supporting the conclusions of this article will be made available by the authors, with anonymization of personal information regarding the patient, without undue reservations.

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