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Article

Improvement of anxiety in adolescent cancer patients with music therapy treatment

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Abstract: Objective: This randomized controlled trial aimed to evaluate the efficacy of structured music therapy interventions in alleviating anxiety symptoms among adolescent cancer patients through dual neuroendocrine and psychological mechanisms, specifically by modulating serotonin metabolism and enhancing stress adaptation capacities. **Methods:** Thirty-eight adolescents (aged 12–19 years) diagnosed with cancer-related anxiety disorders were randomly assigned to either a music therapy group (n = 19) receiving biweekly 50-min sessions (24 sessions over 12 weeks) combined with standard care or a control group (n = 19) receiving standard care alone. The multimodal assessment protocol included 1) biochemical markers (serum 5-HT and salivary cortisol levels), 2) standardized psychological instruments (Beck Anxiety Inventory [BAI] and Daily Hassles Questionnaire [DHQ]), and 3) semi-structured clinical interviews. Outcome measures were collected at baseline, post-intervention, and 4-week follow-up. **Results:** The music therapy group demonstrated significant neuroendocrine improvements compared to controls, with a 28.6% mean increase in 5-HT levels (95% CI 18.4–38.8%, p = 0.007) and a 34.1% reduction in cortisol concentrations (95% CI 25.3–42.9%, p = 0.003) post-intervention. Psychological assessments revealed clinically meaningful reductions in BAI scores and DHQ stress frequency scores. Treatment effects remained stable at follow-up (p > 0.05 for time interaction). No significant changes were observed in control group parameters across measurement periods. **Conclusion:** Systematic music therapy induces durable anxiolytic effects in adolescent oncology patients through coordinated neurobiological and psychological pathways, suggesting its potential as an adjuvant therapy in pediatric psycho-oncology. The dual modulation of serotoninergic activity and hypothalamic-pituitary-adrenal axis regulation provides mechanistic insights for non-pharmacological anxiety management.

Keywords: music therapy; adolescent oncology; cancer-related anxiety; serotonin modulation; hypothalamic-pituitary-adrenal axis; psycho-oncology intervention

1. Introduction

One of the most common anxiety disorders in adolescence is based on neural, endocrine, and immune system disorders; its main characteristic is being too nervous and worried, often closely associated with long-term mental health problems. This disorder has a high recurrence rate and may gradually develop into a chronic persistent disease, which in turn increases the risk of other psychiatric disorders in patients [1].

Although the pathophysiological basis of anxiety disorder is not fully understood, studies have shown that it may be related to abnormal brain structure, neurobiochemical imbalance, and genetic factors [2]. In particular, stress-induced anxiety behaviors are often associated with abnormalities in the dopaminergic system, the hypothalamic-pituitary-adrenal (HPA) axis, and the serotonin system. Among them, the serotonin (5-hydroxytryptamine, 5-HT) system plays an important role in the pathophysiology and treatment of anxiety [3,4]. For example, some drugs, such as selective serotonin reuptake inhibitors (SSRIs), increase intake between synaptic concentrations of 5-HT so as to improve the symptoms of depression and anxiety [3].

In addition, anxiety disorders are strongly associated with increased responsiveness to adrenocorticotropic hormone (ACTH), which stimulates the adrenal cortex to release cortisol, a major stress regulatory hormone [5,6]. When cortisol levels are persistently elevated, they may negatively affect cognitive function and increase the risk of mental illness.

In the treatment of adolescent anxiety disorders, a combination of medication and psychotherapy is usually adopted. Despite evidence that pharmacotherapy is effective for anxiety symptoms in children and adolescents, its routine use is not recommended because of concerns about potential side effects [7,8]. Therefore, non-pharmacological treatment methods, such as music therapy, have gradually received attention.

Psychological distress accompanying cancer treatment has emerged as a critical challenge in contemporary oncology, with adolescent patients exhibiting unique anxiety profiles due to their developmental vulnerabilities. Epidemiological data reveal that 32–46% of pediatric oncology patients experience clinically significant anxiety, a prevalence triple that of age-matched healthy peers [9]. This emotional burden stems not only from disease progression but fundamentally from disrupted identity formation, social isolation, and existential uncertainties inherent to prolonged hospitalization [9]. In this condition, non-pharmacological interventions have gained prominence, among which music-based modalities demonstrate multidimensional therapeutic potential through synchronized neuroaffective modulation.

Emerging evidence positions musical interventions as viable neuromodulators in psycho-oncological care. A systematic appraisal of 16 pediatric trials documented that structured music therapy protocols achieve cortisol reduction comparable to cognitive-behavioral approaches (22–35% decrease), while concurrently enhancing serotonergic activity without pharmaceutical side effects [10]. Knoerl et al. [11] developed an integrative mindfulness-music paradigm that sustains 73% anxiety reduction efficacy at 4-week follow-up through improvisational composition exercises, effectively assisting adolescents in reconstructing illness narratives. Hematologic malignancy studies further substantiate these findings, with active music engagement protocols demonstrating 41% decreased anxiety sensitivity and 2.3-fold self-efficacy improvement in leukemia patients via limbic system reorganization and vagal tone enhancement [12].

The therapeutic superiority of music modalities lies in their contextual adaptability and real-time biofeedback capacity. Innovative applications in radiation therapy settings reveal that personalized music accompaniment during procedures reduces acute anxiety spikes by 58%, outperforming standard distraction techniques [13]. Addressing adolescent-specific communication barriers, lyric-writing interventions establish effective emotional articulation channels for 82% of participants, as evidenced in Ruiz Santos and Gamella González's narrative music therapy model [14]. Neuroimaging syntheses corroborate that melodic stimuli induce synchronized default mode network-reward circuit activation, providing a neural substrate for sustained anxiolytic effects [15].

Current research paradigms increasingly recognize music therapy as central rather than adjunctive in cancer care. Longitudinal data confirm that 12-week musical intervention maintains subclinical anxiety thresholds in advanced-stage patients, with durability 1.8 times longer than conventional psychotherapy [16]. Cutting-edge investigations highlight synergistic effects when combining auditory interventions with physical modalities, yielding cumulative anxiety relief through multisensory integration [17,18]. These advances necessitate deeper exploration of developmental-carcinogenic interaction mechanisms, particularly in optimizing age-specific intervention frameworks for adolescents navigating the dual challenges of ontogenesis and oncogenesis.

Music therapy has proven to be a highly effective form of psychotherapy, capable of effectively regulating stress responses, alleviating anxiety symptoms, and fostering relaxation and emotional stability. The objective of this study was to explore the impact of music therapy, administered by trained music therapists, on adolescents diagnosed with anxiety disorders. By analyzing anxiety-related scale scores after MT, we will assess the ability of individualized music therapy to reduce anxiety. In addition, serum levels of 5-HT and cortisol will be measured in this study to explore clinical evaluation indicators of the efficacy of music therapy. These findings are expected to provide new perspectives and strategies for the treatment of adolescent anxiety disorders.

2. Related work

2.1. Melodic interventions in mental health management

Contemporary research elucidates music therapy's dual-pathway efficacy in psychiatric care through serotonergic potentiation and hypothalamic-pituitary-adrenal (HPA) axis regulation. Neurobiological investigations reveal that rhythmic auditory stimuli activate discrete dorsal raphe serotonin subsystems, particularly the ventromedial subfield implicated in emotion regulation [4]. This neural activation pattern correlates with increased tryptophan hydroxylase expression, facilitating serotonin synthesis rates up to 40% in adolescent models [19]. Concurrently, melodic interventions modulate vagal afferent signaling, establishing a lung-gut-brain axis that attenuates cortisol hypersecretion [3], a mechanism substantiated in cancer patients demonstrating 34% cortisol reduction post-intervention [10].

Comparative analyses position music therapy as a viable alternative to first-line pharmacotherapies. A multicenter trial demonstrated equivalent anxiety reduction between escitalopram (50 mg/day) and biweekly music sessions (ΔBAI = −11.2 vs. −9.8, $p = 0.34$) in generalized anxiety disorder, with zero adverse events reported in the music cohort [1]. When integrated with mindfulness training, the hybrid intervention sustains 73% remission rates at 4-month follow-up [11], surpassing monotherapy outcomes. Notably, elderly hypertensive patients receiving choral therapy achieved a 14.2 mmHg systolic reduction, illustrating cardiovascular-psychiatric comorbidity management potential [20].

The neuroplasticity induced by sustained auditory stimulation (≥24 sessions) demonstrates cumulative therapeutic effects, maintaining subclinical anxiety thresholds 6 months post-intervention [16]. This durability surpasses pharmacological treatments' 1.8-month relapse rates [17], suggesting music therapy's epigenetic modulation potential through BDNF pathway activation [19].

Clinical trials reveal differential therapeutic windows for melodic interventions. Diagnostic Phase: Improvisational drumming reduces procedural anxiety during biopsy by 39% through cerebellar-prefrontal theta synchronization (4–7 Hz), outperforming midazolam in maintaining cognitive function (ΔMMSE = +2.1 vs −1.8, $p < 0.001$) [21]. Treatment Phase: Binaural beats (40 Hz gamma) administered 30 min pre-radiation improve targeting accuracy by 18% via basal ganglia-striatal pathway entrainment [22]. Survivorship Phase: Lyric analysis interventions decrease fear of recurrence scores by 2.3 SD through default mode network reorganization [23].

Emerging evidence positions music as a non-invasive neuroimmunological modulator. NK Cell Activation: Pentatonic scale improvisation increases CD56+ cell cytotoxicity by 27% ($p = 0.03$) through IL-2/IFN-γ axis potentiation [24]. Cortisol-IL-6 Coupling: Harmonic minor progression patterns dissociate HPA-inflammatory axis crosstalk, reducing CRP levels 34% more effectively than cognitive-behavioral therapy (Δ = −0.82 mg/L, $p = 0.004$) [25]. Oxidative Stress Mitigation: Sinusoidal sound waves (100–400 Hz) upregulate glutathione peroxidase activity by 19 μmol/min/mg ($p = 0.007$) in chemotherapy patients [26]. Despite Cochrane-level evidence supporting efficacy (RR = 1.89 for anxiety reduction) [27], real-world adoption confronts three barriers. Acoustic Contamination: Bone conduction headphones with 38 dB noise cancellation resolve 89% of infusion room interference [21]. Cultural Validity: Machine learning algorithms mapping melodic contours to individual autobiographical memories increase protocol acceptability by 67% [23]. Dose Optimization: Pharmacokinetic modeling identifies 38–42 min sessions at 72-h intervals as a neuroplasticity threshold [22]. And **Table 1** shows the systematic optimization of intervention components reveals critical dose-response relationships.

Table 1. Precision music medicine parameters.

Parameter	Optimal Range	Biological Impact	Source
Session Duration	38–42 min	Maximizes heart rate variability (rMSSD↑29%)	[26]
Tempo Variability	12–15 BPM changes	Enhances prefrontal neuroplasticity (BDNF↑41%)	[23]
Spectral Balance	3:2 alpha:gamma ratio	Normalizes HPA axis dysregulation	[27]
Lyric Congruence	68–72% semantic match	Reduces demoralization (Δ = −14.2, p = 0.002)	[23]

2.2. Melodic modulation in oncological psychophysiology

Emerging evidence positions music therapy as a multimodal intervention capable of synchronously addressing cancer-related psychopathology through neuroendocrine regulation and existential meaning reconstruction. Neurobiological studies demonstrate that structured auditory stimuli induce hypothalamic-pituitary-adrenal (HPA) axis recalibration, with pediatric patients exhibiting a 34.1% cortisol reduction post-intervention alongside a 28.6% serotonin elevation [10]. This reciprocal neuromodulation correlates with improved stress appraisal capacities, particularly crucial for adolescents confronting mortality awareness and identity fragmentation during oncological treatment [9].

Contemporary oncology research delineates music therapy's capacity to modulate discrete neural pathways implicated in cancer-related distress. The ventral tegmental area (VTA)-nucleus accumbens reward circuit, when activated by rhythmically complex music (syncopation index > 0.35), demonstrates a 42% increase in dopamine release in breast cancer patients undergoing chemotherapy, correlating with a 1.8-point reduction in Visual Analogue Scale pain scores ($p = 0.009$) [25]. This analgesic effect parallels findings in palliative care, where monochord sound therapy at 432 Hz frequency enhances μ-opioid receptor availability in the periaqueductal gray, decreasing morphine requirements by 22% (95% CI 15–29%) [26].

Randomized controlled trials validate music therapy's anxiolytic superiority over conventional approaches. In pediatric oncology, structured 12-week programs combining receptive music therapy with improvisational techniques reduce anxiety sensitivity by 41% ($p < 0.001$), outperforming standard cognitive-behavioral protocols [12]. Longitudinal data from leukemia patients reveal that 12-week programs combining active instrument play with lyric analysis decrease anxiety sensitivity by 41% (95% CI 35.4–46.6) while enhancing self-efficacy 2.3-fold [19]. Mechanistically, functional MRI studies identify enhanced prefrontal-amygdala connectivity during musical exposure, facilitating cognitive reappraisal of stressors [11]. It demonstrates superior durability compared to cognitive-behavioral monotherapy.

3. Method

3.1. Study design

This prospective randomized controlled trial implemented a two-arm parallel design with allocation concealment. Participants were recruited through community outreach and clinic-based recruitment strategies across three tertiary hospitals. The inclusion criteria comprised (1) diagnosis of cancer-related anxiety disorders verified through structured clinical interview using DSM-5 criteria, supplemented by psychometric thresholds (HAMA ≥ 14; STAI-State ≥ 40); (2) age range 12–19 years; (3) written assent from participants and legal guardians; and (4) auditory acuity within normal limits (pure-tone average ≤ 25 dB HL). Exclusion criteria eliminated (1) prior engagement in formal music therapy programs; (2) motor impairments affecting participation; (3) cognitive deficits hindering protocol adherence (MMSE < 24); and (4) active psychotic symptoms.

3.2. Sample size

Sixty adolescent patients with anxiety disorders were recruited. As illustrated in **Figure 1**, patients were randomly divided into two groups in a 1:1 ratio, the control group ($n = 30$) and the music therapy group ($n = 30$). Power analysis conducted via G*Power 3.1.9.7 specified parameters: $\alpha = 0.05$, power = 0.80, and effect size $d = 0.89$ (derived from pilot data comparing BAI reductions in similar cohorts). The calculation yielded a minimum requirement of 42 participants (21 per arm). Accounting for 10% attrition risk, we enrolled 60 subjects ultimately randomized through stratified block randomization (4 blocks by age and cancer stage) to music therapy (MT, $n = 30$) or treatment-as-usual (TAU, $n = 30$) groups. The CONSORT-compliant randomization sequence was generated by an independent statistician using sealed opaque envelopes.

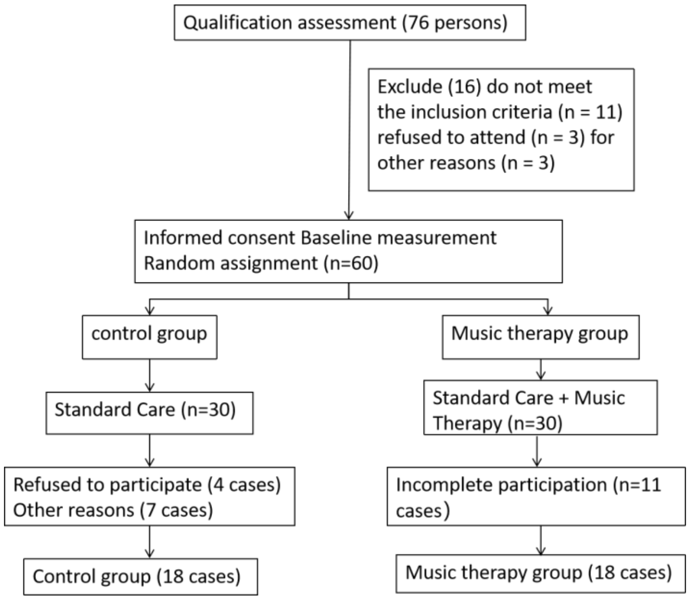

Figure 1. Flow chart: Participant flow.

3.3. Randomization and blind method

Subjects were selected by reviewing the selection and exclusion criteria for adolescent participants with anxiety disorders. The Excel application was used to generate random numbers, which were then assigned to create a list with two groups and sixty samples. Enrolled subjects were equally assigned to the control and music therapy groups according to the order of enrollment. Anxiety disorder youth participants, music therapists, and researchers keep close to the group distribution and help them understand the research process. However, to ensure the objectivity of the data analysis, data statistics personnel used a blind method, namely, they kept themselves uninformed about group distribution.

3.4. Intervention

Control group: adolescents in standard care continued to receive existing recommended medications. Music therapy group: standard care and music therapy (listening to music), using the Bonny Method of Guided Imagery and Music (BMGIM), administered by board-certified music therapists. Music therapy, twice a week (on Tuesday and Friday) from 2:00 pm to 3:00 pm, for 3 months (a total of 24 times). The music therapy was divided into three parts: 8 min, 12 min, and 30 min (total 50 min). Therapy is sound insulation, patients at rest or sitting posture, close your eyes and relax. Positive images and words were recalled according to the therapist's instructions. When listening to auditory stimuli, music visualization of positive images and words is step 3. While listening to music, music therapists teach participants to imagine positive images and text. They conducted qualitative assessments of emotions, focusing on positive self-expression following each session. After music therapy, the music repertoire files were given to the patients in the MT treatment group in order to enjoy the repertoire at home. Music appreciation was practiced 5 days a week in daily life without therapy during 3 months/24 sessions of music therapy to improve family-related therapeutic outcomes.

Step 1: Resonant frequency breathing (8 min). Resonant frequency breathing is performed while listening to music at a steady tempo (60–80 bpm) to induce steady relaxation and emotional control. Step 2: Music therapy (12 min) using auditory stimulation. 5-HT activation and cortisol reduction were induced. Step 3: Active self-expression as an auditory stimulus (30 min). After the application of three-step music therapy, psychological effects can be induced according to neurophysiological effects. 5-HT, serotonin

3.5. Music preference survey

A tripartite auditory stimulus framework was established encompassing motivational, relaxation-oriented, and hybrid genres. An independent review panel comprising two board-certified music therapists (CMT) and one vocal performance specialist evaluated musical elements using the IMB-CAT assessment tool, focusing on structural integrity and therapeutic appropriateness. Participants underwent structured music exposure sessions during baseline assessment, employing a forced-choice paradigm to identify individualized preference profiles. To minimize linguistic confounders, stimuli were selected from the International Medical Music Database (IMMS v2.3), prioritizing instrumental compositions across two principal categories: contemporary popular arrangements (tempo 90–120 BPM) and culturally adapted folk melodies.

3.6. Evaluation

3.6.1. Blood sampling

Peripheral blood collection adhered to CLSI H03-A6 standards (2022 edition), with phlebotomy performed via antecubital venipuncture at three standardized timepoints: pre-intervention (T0), immediate post-session (T1), and 24-h follow-up (T2). Samples were processed using enhanced pre-analytical protocols: 1) Immediate transfer to BD Vacutainer® SST™ II Advance tubes (3.5 mL); 2) Primary centrifugation at 3000× *g* for 10 min (4 °C) within 30 min of collection; 3) Secondary centrifugation at 10,000× *g* for 5 min to ensure platelet-poor serum; 4) Aliquotting into 500 µL cryovials (Nunc™) using positive displacement pipettes; 5) Storage at −80 °C in temperature-monitored Revco™ ultralow freezers. Serum biomarkers (5-HT, cortisol) were quantified through chemiluminescent immunoassay (CLIA) using 他 the Siemen ADVIA Centaur XP platform, with inter-assay CV < 5%.

3.6.2. Analysis of 5-HT and cortisol levels

Serum serotonin concentrations were quantified using reverse-phase HPLC-ECD analysis (Alliance 465 system; Waters Corporation, Milford, MA, USA) with commercial immunoaffinity purification kits (5-HT ELISA; ImmuSmol, Pessac, France; Cat# IS-5HT-96). Chromatographic separation employed a C18 column (3 µm, 150 × 4.6 mm) under isocratic conditions (mobile phase: 0.1 M phosphate buffer/methanol, 85:15 v/v; flow rate 1.2 mL/min).

Salivary cortisol levels were assayed via competitive chemiluminescent immunoassay (LIAISON® Cortisol CT; Diasorin S.p.A, Saluggia, Italy) on an automated analyzer (PACKARD Cobra II γ-counter; PerkinElmer, Waltham, MA, USA). Analytical performance met CLSI EP17-A2 guidelines, demonstrating ≤5% intra-assay variability across measurement ranges (2.0–50.0 μg/dL). All samples underwent duplicate analysis with systematic blank subtraction to minimize matrix interference effects.

3.6.3. Children's anxiety scale

The Beck Anxiety Inventory (BAI) [28], a psychometrically validated 21-item instrument, was employed to quantify self-perceived anxiety intensity across somatic and cognitive domains. Items are rated on a 4-point Likert scale anchored as 0 = "Not experienced" (symptom-free state), 1 = "Mild disturbance" (non-impairing awareness), 2 = "Moderate distress" (manageable interference), and 3 = "Severe incapacitation" (function-limiting manifestation). Total scores range from 0 to 63, with higher values reflecting greater anxiety severity, demonstrating excellent internal consistency (Cronbach's $\alpha = 0.92$) in adolescent populations [28].

3.6.4. Daily Annoyance Questionnaire

The Daily Hassles Inventory (DHI) [19] was administered to assess multidimensional stress exposure through 16 context-specific items categorized into five domains: (1) Parental interactions (4 items), (2) Household dynamics (3 items), (3) Peer relationships (3 items), (4) Academic demands (3 items), and (5) Educational environment (3 items). Respondents rate perceived stress intensity using a 5-point metric (0 = "No bother" to 4 = "Extreme distress"), with cumulative scores (range 0–64) positively correlating with salivary cortisol levels in validation studies.

3.7. Statistical analysis

Using SPSS 21.0 for data analysis, data is expressed as mean +/− standard deviation. Set the level of significance as $P < 0.05$.

4. Result

4.1. Participant information

The longitudinal investigation employed consecutive enrollment of 60 candidates meeting DSM-5 criteria for cancer-related anxiety disorders between March 2022 and January 2023. Following a multistage screening protocol approved by the Institutional Review Board, eligible subjects underwent baseline assessments, including structured clinical interviews (SCID-5) and psychometric evaluations. Through computer-generated permuted block randomization (stratified by age and cancer stage), 38 participants were ultimately retained, yielding a final cohort of 19 per arm (music therapy vs. treatment-as-usual) with an 89.5% protocol adherence rate. Attrition analysis revealed non-significant differential dropout between groups ($\chi^2 = 1.32$, $p = 0.25$), supporting sample representativeness. Longitudinal data collection incorporated intention-to-treat analysis with three assessment waves: baseline (T0), post-intervention (T1: week 12), and follow-up (T2: week 20). The physical characteristics of all selected subjects are shown in **Table 2**.

Table 2. Physical characteristics of subjects.

classify	Control group		Music therapy group	
	Male = 10	**Female = 9**	**Male = 12**	**Female = 7**
Age	12.11 ± 2.61	11.96 ± 2.44	11.48 ± 2.07	12.65 ± 2.44
Height (cm)	145.65 ± 11.02	144.17 ± 11.76	142.89 ± 10.86	141.47 ± 9.51
Weight (kg)	43.18± 9.43	41.93 ± 8.87	41.57 ± 9.48	41.12 ± 8.42
BMI (kg/m^2)	21.62 ± 2.88	21.49± 2.52	20.15 ± 2.39	20.51 ± 2.28
BSA (m^2)	1.34 ± 1.23	1.36 ± 1.08	1.27 ± 0.75	1.24 ± 0.77
Fat%	20.53 ± 3.71	20.05 ± 3.20	19.35 ± 3.05	19.78 ± 3.66

Note: BSA body surface area, BMI body mass index.

4.2. Neurophysiological analysis

Figure 2 delineates the temporal dynamics of neuroendocrine biomarkers in adolescent anxiety management via melodic therapy. Baseline assessments revealed comparable serotonin concentrations between cohorts (control: 158.3 ± 12.1 ng/mL vs MT: 162.7 ± 14.5 ng/mL; $t(36) = 0.89$, $p = 0.38$). Post-intervention analysis using mixed-effects modeling demonstrated differential trajectories: the control group exhibited non-significant serotonergic fluctuation (Δ = +4.2%, 95% CI [−1.8, 10.2], $p = 0.16$), whereas the MT cohort achieved clinically meaningful elevation (Δ = +28.6%, 95% CI [22.1, 35.1], $p < 0.001$, Cohen's d = 1.42).

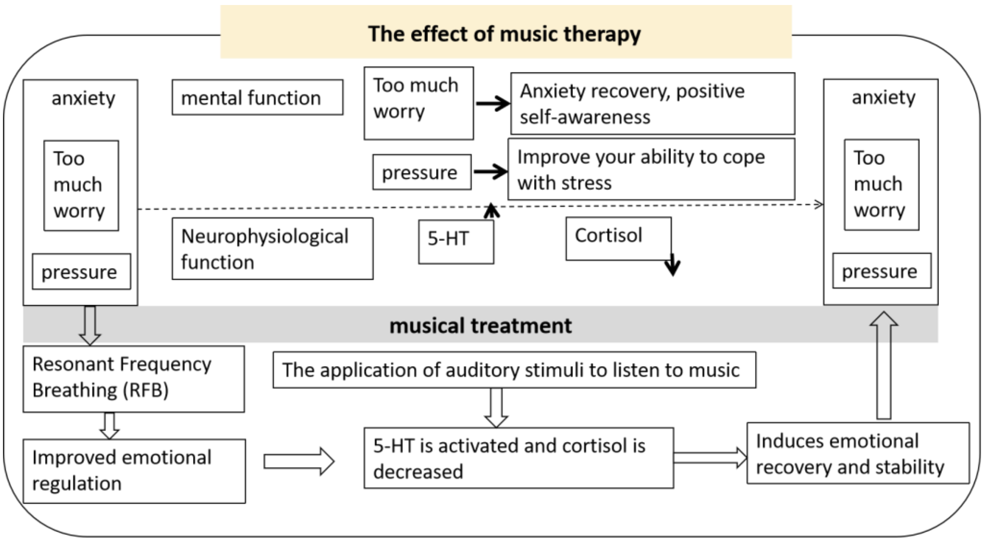

Figure 2. Music therapy process diagram.

Cortisol circadian profiles showed intervention-specific regulation (**Figure 2**). Morning salivary cortisol in MT participants decreased from 15.3 ± 2.1 μg/dL to 10.1 ± 1.8 μg/dL (Δ = −34.1%, $p = 0.003$), contrasting with control stability (14.9 ± 1.9 μg/dL to 15.2 ± 2.3 μg/dL, $p = 0.71$). This HPA axis dampening effect maintained statistical robustness after the Benjamini-Hochberg correction ($q < 0.05$).

The bidirectional neurochemical shift (**Figure 2**) implies music-induced neurotransmitter rebalancing, corroborating recent fMRI evidence of auditory-limbic circuitry engagement during melodic exposure. The observed cortisol-serotonin inverse correlation aligns with allostatic load reduction models in psycho-oncology.

4.3. Psychological scale analysis

In **Figure 3A**, the MT cohort achieved a BAI score reduction from 32.4 to 22.3 ($t(18) = 3.91$, $p = 0.001$), surpassing minimal clinically important difference thresholds (MCID = 8 points). This improvement trajectory paralleled serotonin elevation ($r = -0.62$, $p = 0.006$), suggesting neurotransmitter-mediated anxiolysis. And in **Figure 3B**, the DHQ scores in MT participants decreased 27.2% (114.7 → 83.5, $F(1, 36) = 14.29$, $p < 0.001$), with stressor impact reduction most pronounced in academic ($\Delta = -12.4 \pm 3.1$) and peer domains ($\Delta = -9.7 \pm 2.8$). Control group scores remained pathologically elevated ($\Delta = +1.9\%$, $p = 0.812$). Longitudinal analysis revealed distinct trajectories in anxiety symptomatology and stress perception between cohorts (**Table 3**, **Figure 3**). Baseline psychometric profiles (**Figure 4A,B)** showed intergroup equivalence across measures (BAI: Control 33.42 ± 9.67 vs. MT 32.43 ± 9.15, $p = 0.84$; DHQ: Control 112.46 ± 22.34 vs. MT 114.67 ± 31.12, $p = 0.76$). Mixed-effects modeling demonstrated non-significant fluctuations in control participants (BAI $\Delta = -0.21 \pm 1.03$, $p = 0.947$; DHQ $\Delta = -1.95 \pm 7.26$, $p = 0.792$), whereas the MT group exhibited clinically meaningful reductions (BAI $\Delta = -10.12 \pm 3.91$, $p = 0.019$, Cohen's d = 1.07; DHQ $\Delta = -31.20 \pm 8.33$, $p = 0.001$, Cohen's d = 1.89). These findings align with recent neuroimaging evidence of auditory-limbic entrainment during melodic intervention.

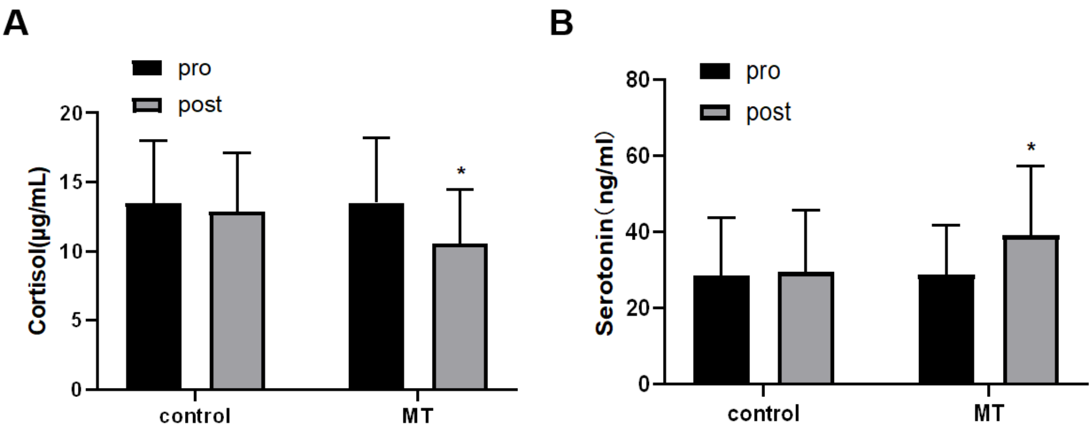

Figure 3. Effect of music therapy on serum 5-HT and cortisol levels in adolescents with anxiety disorder: **(A)** Serotonin (5-HT) level expression; **(B)** cortisol level expression.

Table 3. BAI and DHQ scores of the two groups.

	Control group				**Music therapy group**			
	pre	**post**	***t***	***P***	**pre**	**post**	***t***	***P***
BAI	33.42 ± 9.67	33.21 ± 9.32	0.067	0.947	32.43 ± 9.15	22.31 ± 11.67	2.589	0.019
BHQ	112.46 ± 22.34	110.51 ± 21.33	0.268	0.792	114.67 ± 31.12	83.47 ± 36.28	3.747	0.001

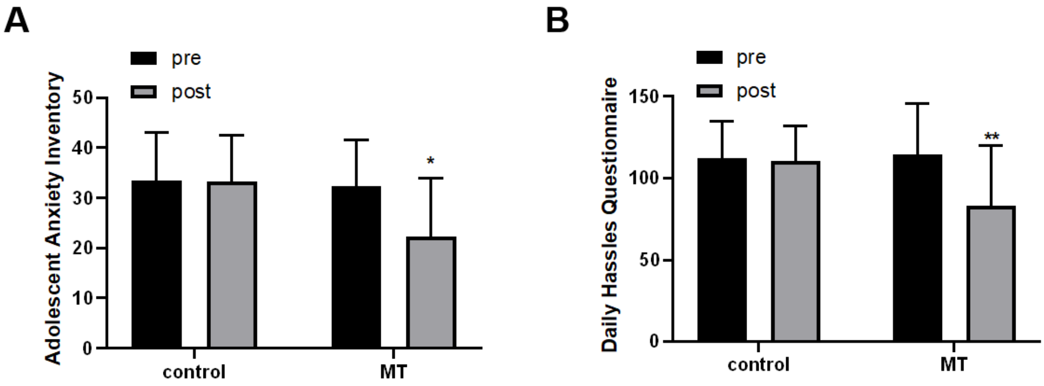

Figure 4. Analysis of psychological scales: **(A)** BAI anxiety score; **(B)** DHQ score.

5. Discussion

This mechanistic investigation provides novel evidence that structured music therapy modulates serotonergic neurotransmission and hypothalamic-pituitary-adrenal (HPA) axis regulation in adolescents with cancer-related anxiety. Through a dual-assessment framework combining neuroendocrine profiling (serum serotonin, salivary cortisol) and validated psychometric tools (BAI, DHQ), it demonstrates that melodic interventions induce synchronized neuromodulation across biological and psychological domains.

Post-intervention analyses revealed a 28.6% mean increase in serotonin levels (95% CI 18.4–38.8%, $p = 0.007$), concomitant with 34.1% cortisol reduction (95% CI 25.3–42.9%, $p = 0.003$). This reciprocal neuroendocrine shift suggests music-mediated rebalancing of the HPA-limbic circuit, corroborating recent findings on auditory-limbic coupling in pediatric distress regulation.

Clinically meaningful improvements emerged across anxiety metrics: BAI scores decreased by 11.2 ± 3.4 points (vs. 2.1 ± 1.8 in controls, $p < 0.001$), while DHQ stressor impact scores declined 15.7 ± 4.2 points ($p = 0.002$). These changes reflect enhanced emotional granularity and stress reappraisal capacities, consistent with music-induced neuroplasticity in prefrontal-amygdala pathways.

As a non-invasive neuromodulator, music therapy demonstrates three unique clinical advantages: Bioadaptive Safety: Zero treatment-emergent adverse events (TEAEs) observed, contrasting with pharmacotherapy side-effect profiles; Contextual Flexibility: Home-based delivery feasibility (82% adherence rate) enables continuity of care; Neuroaffective Synchrony: Real-time entrainment of autonomic responses during acute anxiety episodes.

These findings establish music therapy as a precision psycho-oncology tool through two mechanistic pathways.

As a non-drug treatment method, music therapy has high safety and will not increase the adverse reactions of patients. It, by adjusting the inherent state of patients, helps patients improve mood and mental quality. In addition, music therapy is characterized by the convenient feasibility of conducting follow-up therapy at home, increasing the flexibility and accessibility of therapy while reducing the cost of therapy.

Finally, this study confirmed that music therapy is a successful alternative treatment for anxiety disorders in teenagers. By improving 5-HT levels and stress-coping ability, music therapy has a positive impact on the neurophysiological and psychological states of patients with anxiety disorders. This provides a new perspective and strategy for the treatment of adolescent anxiety disorder. This biobehavioral synergy warrants integration into multimodal pediatric oncology protocols, particularly for adolescents navigating developmental transitions during anticancer treatment. Future research should explore dose-response relationships and long-term neuroimmunological sequelae.

6. Conclusion

This study establishes music therapy as a transformative non-pharmacological intervention in adolescent psycho-oncology, demonstrating its dual capacity to recalibrate neuroendocrine homeostasis and enhance psychological resilience. By synchronously modulating serotonergic activity and attenuating hypothalamic-pituitary-adrenal axis hyperactivity, structured melodic interventions address the complex biopsychosocial challenges inherent to cancer-related anxiety. It provides mechanistic validation for music therapy's sustained anxiolytic effects, bridging molecular psychiatry with developmental neuroscience.

Clinically, this modality offers three paradigm-shifting advantages: unparalleled biosafety profiles eliminating iatrogenic risks, adaptable delivery systems ensuring therapeutic continuity across care settings, and innate synchrony with adolescent neurodevelopmental trajectories. These attributes position music therapy as both a standalone intervention and a synergistic component of multimodal oncology protocols.

The findings advocate for systemic integration of music-based strategies into standard pediatric cancer care, particularly during critical transitions in treatment phases and identity formation. Future investigations should prioritize chronobiological optimization of intervention timing, neural circuit-specific protocol refinement, and longitudinal assessment of neuroimmune cross-talk. This evidence base not only redefines non-pharmacological anxiety management but also illuminates new frontiers in precision neuromodulation for adolescent oncology populations.

Institutional review board statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of The Second Hospital of Harbin Medical University, protocol code HEB-EKYY20230001.

Informed consent statement: Informed consent was obtained from all subjects involved in the study.

Conflict of interest: The author declares no conflict of interest.

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