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The Effects of Music Therapy on Cortisol Levels as a Biomarker of Stress in Children

Idyatul Hasanah and Zikrul Haikal

Abstract

Stress is a physiological and psychological response to the perception of danger and threat. Stress can occur due to a physical injury, mechanical disturbance, chemical change, or emotional factor. Stress can occur at all ages, including children and adolescents. Various physical and psychological events can cause stress in children, for example suffering from an illness, injury/trauma, parental divorce, parental death, sexual abuse, natural disasters, war, etc. Various exposures to physical and psychological stress harmful to the body can cause it to carry out defense mechanisms against these threats, one of which is changes in the cortisol hormone. Cortisol hormone is used as a biochemical marker for acute and chronic stress. The increase in this hormone as an indicator of stress can be changed through psychosocial interventions, one of which is by the provision of music therapy. Music therapy can manage stress problems of people at various ages with minimal side effects and a small amount of money. It is also easy to apply and does not require any intellectual ability to interpret. There are no limitations for users to use music therapy.

Keywords: Music therapy, cortisol, stress

1. Introduction

Stress is a physiological and psychological response to the perception of danger and threat [1]. Stress can occur due to a physical injury, mechanical disturbance, chemical change, or emotional factor known as stress exposure. The body's response to these factors depends on the magnitude of the stress exposure, the duration of the event, and the patient's nutritional status [2]. Stress can occur at all ages, including children and adolescents. Various physical and psychological circumstances can cause stress in children, for example, the presence of an illness, injury/trauma, parental divorce, parental death, sexual abuse, natural disasters, war, and so on [3].

Exposure to stress can affect almost all aspects of life, i.e., physiological, psychological, cognitive, and social. Some of the symptoms of stress that appear physically include: increased vital signs, vascular vasodilation, increased sweat production, decreased immune system, complaints of headaches, abdominal pain, and increased neurohormonal responses (cortisol, epinephrine, vasopressin). Psychologically, the symptoms of stress include mood disorders, emotions, anxiety, eating disorders, sleep disorders, low self-esteem, ineffective coping, and irritability. In terms of the cognitive aspect, stress can appear in the form of impaired

concentration and memory. Regarding a social aspect, the example of symptoms is impaired interpersonal function such as fear or suspicion, dislike of others, withdrawal, low self-esteem, low self-confidence, affecting relationships and interactions with others [1, 4, 5].

Various exposures to physical and psychological stress harmful to the body can cause it to take defensive actions to overcome the stress. One of the body's responses as a defense against stress is the constant release of stress hormones, including cortisol [1, 4].

Cortisol hormone is used as a biochemical marker for acute and chronic stress [6]. In addition to the increase in cortisol levels, the secretion of epinephrine and vasopressin will also increase due to exposure to stress, thus causing an increase in blood pressure and pulse [1].

Increased cortisol levels as an indicator of stress can be changed through psychosocial interventions. One of the psychosocial interventions often used to manage stress is music therapy [7]. It is an effective complementary approach to manage stress in children, which can achieve specific therapeutic results with minimal side effects in the clinical management of pediatric patients [8, 9]. For children and adolescents, listening to music in various health care contexts is considered feasible, easy to apply, and cost-effective [10].

The effectiveness of music therapy in reducing stress levels in children has been widely reported. It positively impacts reducing pain, heart rate, respiratory rate, and anxiety in children undergoing medical treatment. It can reduce the risk of increased Post Traumatic Distress Syndrome (PTSD) [11–14]. This chapter will review the effect of music therapy on salivary cortisol levels as a biomarker of stress in children.

2. Music therapy

2.1 Definition

Music therapy is a complementary approach by using music to help someone with various health conditions that can affect their physiology, psychology, and emotion [8, 9, 15, 16]. This therapy can manage stress problems of people of different ages with minimal side effects and a small amount of money. It is easy to apply and does not require the intellectual ability to interpret. There are no limitations for users to use music therapy.

Music therapy can generally be divided into two categories, i.e., active and passive. Active music therapy – in which patients play music, sing, or in some way – is encouraged to create or describe their experiences with music. While passive music therapy is a method in which the patient only listens to live or prerecorded music. In surgical and cancer patients, passive forms of therapy are recommended because this type of music therapy can be easily incorporated into clinical situations that involve minimal equipment and staff attention. The patient listens to relaxing music of their choice. It has a profound effect on stress and anxiety levels [17].

2.2 Benefits of music therapy

Music therapy can effectively help children adjust to a hospital environment. Children are usually not familiar with the hospital environment. Many new and scary things may happen in a child's life. Music therapy can be used to intervene for emotional state control, pain management, cognitive processing, and stress management [18, 19].

Music therapy positively affects physiological aspects (such as heart rate, blood pressure, oxygen saturation, and pain). It also positively affects the psychosocial behavior (such as anxiety) of hospitalized children [20]. This therapy reduces postoperative stress and pain in children by improving cardiovascular parameters and improving stress-induced hyperglycemia [21].

Music therapy is often combined with other techniques to improve anesthesia, analgesia, and relaxation. While live music sessions with a music therapist are considered most effective, this may not be possible in an environment or institution that does not have a trained professional therapist. Therefore, recorded music can be a choice.

2.3 Factors that can affect the effectiveness of music therapy in children

Characteristics of good music for pediatric patients are that the decibel level of musical stimulation should be 35–85 dB. Music stays in the soft to medium-volume range. The rhythm should also be regular, without sudden fluctuations in tempo. The use of headphones has several advantages, especially in critical care, including improving hearing at an acceptable decibel level, attention to ambient noise, and lower effect on other patients [8]. Several factors affecting the effectiveness of music therapy are as follows:

2.3.1 Environmental disturbance

Environmental disturbances can reduce the effectiveness of music therapy or even have a negative impact. Examples of such environmental disturbances are noise caused by people passing by, talking, crying, or shouting when music therapy is given.

Environmental noise can interfere with the effectiveness of music therapy even though earphones/headphones are being used [8]. This is probably brought about by the activeness of other senses (e.g., sight), which can still receive stimuli from the environment. The effect of uncontrollable noise levels during music therapy resulted in no positive impact of music therapy on neuroendocrine responses (cortisol levels) to stress [22].

2.3.2 Type of music and duration

Music therapy can provide direct benefits to patients regarding the physiological, psychological, and socio-emotional aspects [23]. An important factor that can increase the effectiveness of music therapy is the type of music that is based on the patient's choice (preferences), songs that are usually heard (familiarity), cultural context, and past experiences [8, 24]. In addition, letting the patient set the frequency, duration, and timing of the music intervention directly is the best approach in providing music therapy [25]. Giving music therapy more than 20 minutes can negatively impact children's stress levels, which can be seen from their cortisol levels [26].

2.3.3 Type of diagnosis and level of treatment

The type of diagnosis and level of treatment can influence the level of fatigue and stress in children and adolescents with cancer [27]. In pediatric cancer patients who experience fatigue, non-pharmacological therapy, including music therapy, is not very significant [28].

3. Cortisol as a biomarker of stress

Stress measurement through hormone examination in determining a person's emotional status is objective. This method is quite beneficial for pediatric patients who have not been able to express their feelings. It can identify stressful conditions in a person's body that are not visible to the naked eye. As previously explained, one of the hormonal responses to stress is an increase in cortisol as a self-defense effort. Elevated cortisol levels are a good indicator for someone experiencing acute stress or chronic stress [29]. Cortisol can be detected through a saliva test. Salivary cortisol examination is better, more effective, and more valid than blood examination to assess adrenocortical function [30, 31]. The advantages of using salivary cortisol are easy sampling, non-invasive, fast, and repeatable. It also does not require special equipment and can be performed outside the laboratory [32]. Over the past 20 years, salivary cortisol has become the most popular biomarker used in stress studies.

3.1 Cortisol physiology

Cortisol is the main glucocorticoid hormone produced by humans. Glucocorticoids increase blood glucose levels by counteracting insulin secretion and action to inhibit peripheral glucose uptake, promoting hepatic glucose synthesis (gluconeogenesis) and hepatic glycogen levels [33]. The main functions of cortisol are to control carbohydrate, protein, and fat metabolism, suppress inflammatory tissue processes in response to injury, suppress immune responses to foreign antigens, and increase the body's ability to withstand various harmful stimuli (stress) [34].

Cortisol secretion by the adrenal cortex is controlled by a negative feedback system involving the hypothalamus and anterior pituitary. Adrenocorticotrophic Hormone (ACTH) from the anterior pituitary stimulates the adrenal cortex to secrete cortisol. The cells that produce ACTH, in turn, only work following orders from Corticotropin-Releasing Hormone (CRH) from the hypothalamus. The feedback control loop is complemented by the inhibitory effect of cortisol on CRH and ACTH secretion by the hypothalamus and anterior pituitary. The negative feedback system for cortisol maintains a relatively constant level of cortisol secretion. Two additional factors that influence plasma cortisol concentrations in the basic negative feedback control system are diurnal rhythm and stress, both of which react on the hypothalamus to vary the level of CRH secretion [1]. The control of cortisol secretion is shown in **Figure 1**.

3.2 Cortisol circadian rhythm

In the absence of stress exposure or under normal conditions, cortisol secretion exhibits a distinct circadian rhythm when concentrations are highest in the morning (circadian peak), progressively decline from late afternoon to early nocturnal periods (circadian trough), and show a sudden increase after the first few hours of sleep [36]. The circadian rhythm of cortisol can be seen in **Figure 2**.

Normal cortisol in children follows a pattern similar to the circadian pattern in adults, decreasing from 11.00 am to 4.00 pm [37]. The normal range of salivary cortisol levels is between 0.2–11.3 ng/ml. An increase or decrease in salivary cortisol levels is considered significant if there is a difference in 0.05 ng/ml [38].

3.3 Factors affecting cortisol secretion

The interpretation of elevated cortisol can consider several factors (shown in **Table 1**) that can influence it. Infectious factors such as viral infections are also

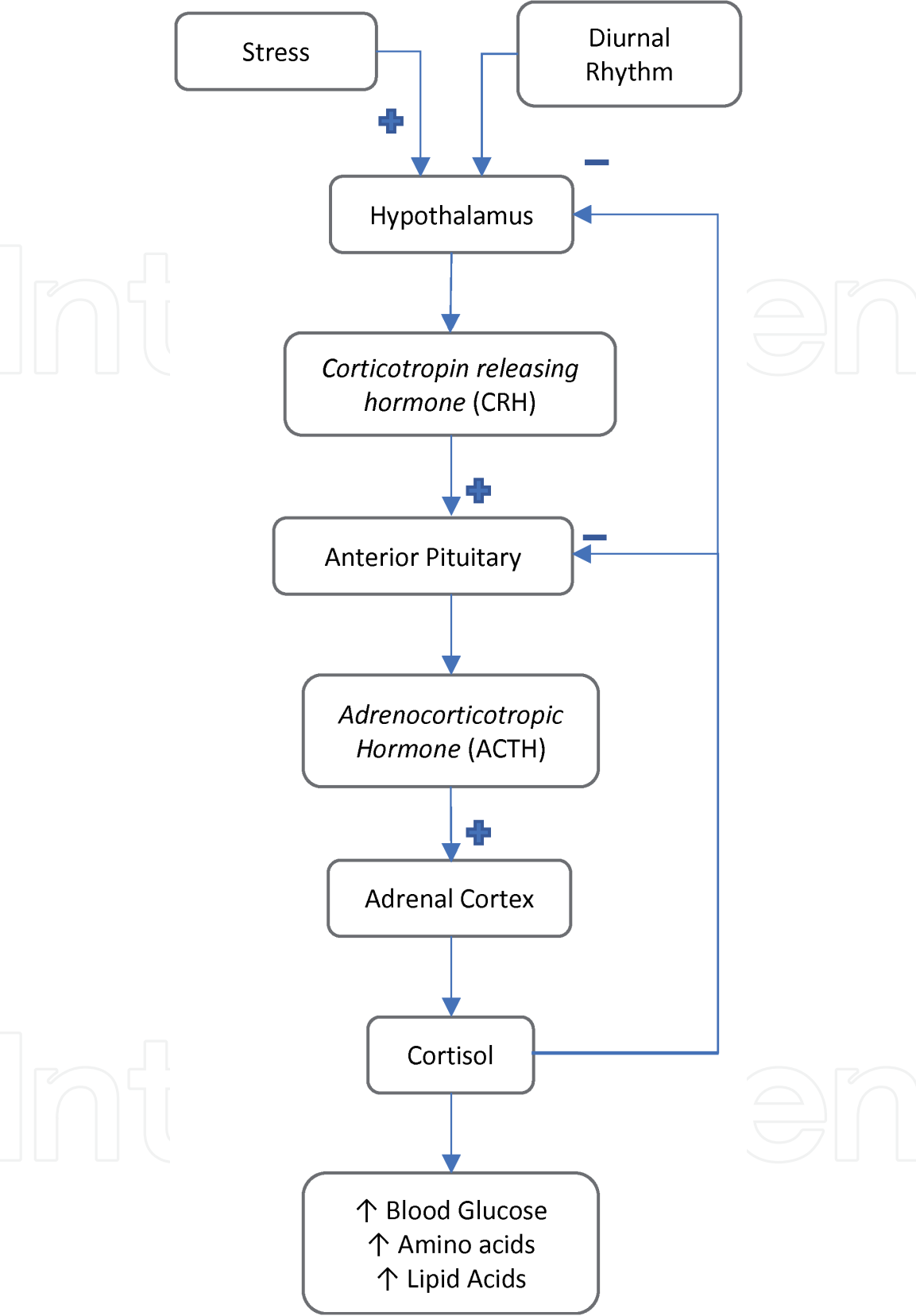


Figure 1.
Control of cortisol secretion [35]. Cortisol secretion is influenced by stress and diurnal rhythms. Increased cortisol in the blood will provide negative feedback on the hypothalamus and anterior pituitary to reduce cortisol secretion.

considered to affect increasing cortisol levels in the body [41]. Elevated cortisol occurs concomitantly with high C-Reactive Protein (CRP) and procalcitonin (PCT) in patients with fever without severe sepsis [42]. A person's symptoms and stress levels are closely related to physical suffering and psychological characteristics [43]. Thus, high cortisol levels are also associated with disability [26, 44].

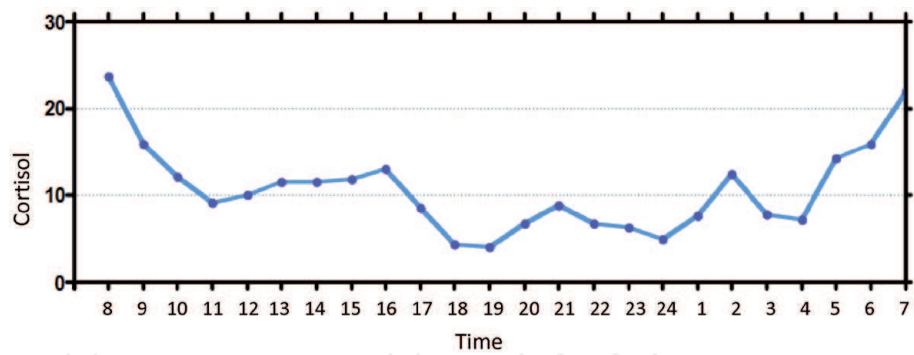


Figure 2. Circadian rhythm of cortisol [36]. Concentrations are highest in the morning (circadian peak), decline steadily from late afternoon to early nocturnal periods (circadian trough), and show a sudden increase after the first few hours of sleep.

Factors affecting	Description
Individual factors including age, gender, and race	<div>a. Cortisol levels increase with age, especially in the elderly. Besides, cortisol reactivity to stress differs depending on age.</div> <div>b. Gender does not affect basal cortisol, but there is a difference in experimental stress exposure.</div> <div>c. The research studied the influence of race on cortisol levels shows varying results. Further research is needed to determine for sure the effect of race on cortisol levels.</div>
Somatic factors	<div>a. Acute and chronic diseases, endocrine and autoimmune diseases.</div> <div>b. Use of drugs (glucocorticoids, anticonvulsants such as phenytoin and carbamazepine, and opioid drugs)</div> <div>c. Obesity</div>
Lifestyle factor	<div>a. Sleep patterns</div> <div>b. Food intake (especially lunch)</div> <div>c. High-protein foods</div> <div>d. Caffeine consumption (regular caffeine consumption increases the activation of the HPA axis, especially during the day) [40]</div> <div>e. Smoking</div> <div>f. Alcohol consumption</div> <div>g. Physical activity.</div>
Psychosocial factors	Exposure to acute and chronic psychosocial stress

Table 1. Factors affecting cortisol secretion [39].

Acute pain from mechanical, chemical, or thermal stimulation will release chemical mediators in the periphery that initiate the pain. Transient activation of peripheral nociceptive fibers sends pain signals through the dorsal horn of the spinal cord to the brain, where the pain signal is perceived. Stress from perceived pain can cause the release of stress hormones such as cortisol [45]. The slightest medical procedure can cause pain and distress in children [46]. Medical actions against the children’s wishes, such as accidental removal of an IV needle and repeated needle sticking, can result in higher distress [26]. This can directly impact extreme physiological symptoms such as vasovagal responses, heart rate changes, stress hormones (cortisol and corticotrophin), and ECG [47, 48].

A sharp increase in cortisol secretion mediated by the central nervous system through increased activity of the CRH-ACTH-Cortisol system occurs in response to all kinds of stressful situations [1]. The magnitude of the increase in cortisol concentration is generally proportional to the intensity and extent of the stress stimulus. More significant increases in cortisol levels are elicited in response to severe stress. Music therapy is a complementary therapy that can be used to reduce the stress response. Still, for the previously mentioned conditions, music therapy does not positively impact the patient. Giving music therapy to individuals with extreme increases in cortisol levels may have minimal or no effect.

4. The effects of music therapy on cortisol levels

Children with health problems often require painful procedures to diagnose or treat their illness. Treatment of the disease may result in the child having to undergo a series of invasive procedures regularly. The most commonly performed invasive procedure is an intravenous puncture. This puncture can cause pain, resulting in stress, such as behavioral responses including crying, vomiting, verbal complaints, and physiological responses, including increased blood pressure, increased stress hormones, muscle tension, and sweating [49].

Physiological responses are controlled by the HPA axis and the sympathetic and parasympathetic components of the peripheral nervous system. The HPA axis interacts with stress-activating centers in the brainstem and hypothalamus and releases Corticotrophin Releasing Hormone (CRH), which is one of the main effects of the stress reaction. CRH stimulates the anterior pituitary to secrete ACTH, and increased ACTH secretion can stimulate the adrenal cortex to increase cortisol secretion [50]. Most studies support the cortisol response to both acute and chronic stress [51].

Cortisol is an objective biomarker associated with general psychological status. It can be used primarily to evaluate children's physiological reactions under stress exposure [52]. Stress is associated with increased production of the cortisol hormone, which is known to suppress the immune response [53].

Control of cortisol activity can be altered through psychosocial interventions [7]. Music therapy is a psychosocial intervention that is safe, easy, economical, and feasible to use and has the benefit of reducing cortisol levels as a stress biomarker in pediatric patients. Music is considered as an adjunct therapy in clinical situations causing pain or anxiety [54]. Several studies have shown the effectiveness of music therapy to reduce cortisol as a stress biomarker in pediatric patients. Furthermore, listening to music can reduce subjective stress levels, decrease salivary cortisol secretion, and increase salivary alpha-amylase activity, which is higher [26, 55]. In addition, music therapy has a positive effect in controlling salivary cortisol concentrations, systolic and diastolic pressure, heart rate, body temperature in anxious dental patients [56]. Listening to soft, relaxing music for an hour in the postoperative period has beneficial effects on the stress response, such as a much more significant reduction in cortisol levels [57].

The mechanisms underlying the effects of listening to music on stress levels are still being studied. There are three possible mechanisms. First, the regulation of activity in the mesolimbic dopaminergic system by music (primarily based on increased activity in the ventral tegmental area and nucleus accumbens with corresponding reactions to stress and pain). Second, the downregulation of amygdala central nuclear activity by music with a down-regulatory effect on fear and worry levels and activity of hypothalamic and brainstem nuclei involved in endocrine generation (HPA axis), and vegetative stress responses (such stress-related effects may also include modulation of beta-endorphin levels). The sound of music that has

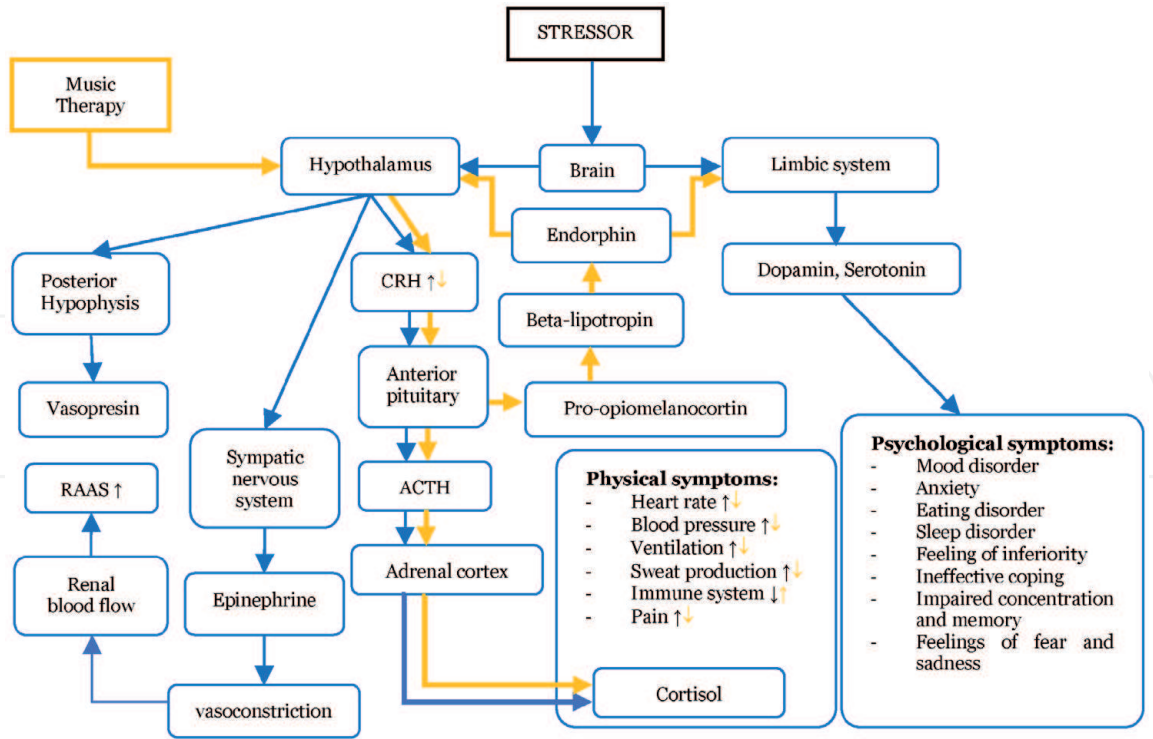


Figure 3.
Mechanism of music therapy in reducing cortisol and stress levels.

been received and perceived by the brain will stimulate the hypothalamus, which will then prompt the pituitary to produce endorphins. Endorphins are endogenous opiates (morphine) that function as the body’s natural analgesics and protect/relieve the body from stressful conditions [1, 58]. Endorphins are mainly synthesized and stored in the anterior pituitary from the precursor protein proopiomelanocortin (POMC). POMC is a large protein broken down into smaller proteins such as beta-endorphin, alpha-melanocyte-stimulating hormone (MSH), adrenocorticotropin (ACTH), etc. The pituitary synthesizes POMC in response to signals from the hypothalamus (in the form of corticotropin-releasing hormone (CRH)). When POMC cleavage protein products accumulate in excess, a negative feedback loop suppresses CRH production in the hypothalamus, thereby decreasing the secretion of stress hormones, including cortisol [59]. Third, music affects the participants’ cognitive resources (including attention) in the patients given the music intervention (**Figure 3**) [58, 60].

Music therapy is not adequate for specific conditions such as fever, the severity of infection, disability, children with cancer with relapse, repeated needle sticking, etc. A person in these conditions usually has extreme levels of cortisol. Music therapy is not effective, even has a negative impact if given when a person has excessive cortisol levels [26].

When a person has a fever, music therapy becomes ineffective in lowering cortisol levels. The cortisol hormone will directly increase when you have a fever. This happens because Cortisol Binding Globulin (CBG) is a thermocouple protein. It is a protein that is sensitive to temperature changes and will release cortisol in response to fever [61]. The cortisol hormone as a biomarker of stress will increase when children with fever are given music therapy [26].

5. Conclusions

Various physical and psychological events can be a cause of stress in children. This stressful condition can be identified through an increase in cortisol levels.

Increased cortisol level is considered the best indicator to determine a person's stress condition, both acute and chronic. The cortisol examination method can be carried out through saliva and blood. Cortisol examination through saliva is much better, more effective, and more valid than cortisol analysis through blood. Besides, this examination is more beneficial in children because it does not cause pain.

The increase in cortisol as an indicator of stress can be changed through psychosocial interventions, one of which is the provision of music therapy. Music therapy can manage stress problems in various ages with minimal side effects and a small budget. It is easy to use and does not require the intellectual ability to interpret. There are no limitations for users to use music therapy. However, several things must be considered before the therapy is given, for example, environmental conditions when the therapy is provided, adjustment of music type, the duration for pediatric patients (should be less than 20 minutes), and the severity of the disease experienced by the patient.

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Conflict of interest

The authors declare no conflict of interest.

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