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Article type : Original Article

Effectiveness of a music intervention on pruritus: an open randomized prospective study

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This article has no funding source.

Conflict of interest: none

Abstract: 300 (words count)

Text: 2525 (words count)

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/jdv.16149](https://doi.org/10.1111/jdv.16149)

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References: 26

Figures: 3

Table: 2

Key-words: pruritus, itch, music intervention, skin diseases, psoriasis, atopic dermatitis

ABSTRACT

Background: Pruritus is a common symptom in many skin diseases. Music interventions have demonstrated their efficacy in different symptoms or diseases such as pain, depression, anxiety.

Objective: To evaluate the effects of a music intervention on pruritus.

Patients and methods: A randomized controlled trial was conducted from November 2018 to April 2019. Fifty inpatients with pruritus intensity $\geq 3/10$ in various chronic skin diseases were randomized in a music group or an emollient group. The primary endpoint was the evolution of pruritus as measured by the Numerical Rating Scale before and one hour after the procedure. The secondary judgement criteria were the effects on patient anxiety, the impact of pruritus on the quality of life, and patient satisfaction (NCT 03701971).

Results: Fifty patients with chronic pruritus were included, 62% were male, the average age was 60.7 years. The most common diseases were psoriasis (N=10), atopic dermatitis (N=8), contact eczema (N=6). The average ItchyQoL score was 64.8/110, showing a significant impact on quality of life. The intensity of pruritus decreased more significantly in the music intervention group than in the emollient group: 2.3 (SD 2.1) and 1.2 (SD 1.7), respectively ($p < 0.05$). There was a decrease in anxiety in both groups, with no statistical significant difference between groups. Among patients who received the music intervention, 64% reported feeling an improvement, 91% would recommend the music intervention, 64% would like to continue this practice.

Discussion: Pruritus management is complex and requires first-line aetiological treatment. Aetiological or symptomatic treatments do not always provide enough relief; it is useful to find other therapeutic options. The music intervention has shown interest in our study. Its repeated use over the long term will be interesting to evaluate. As in pain, music may work by activating inhibitory neural circuits. The use of music is a simple method to manage chronic pruritus.

INTRODUCTION

Pruritus is an unpleasant sensation that causes an urge to scratch. Like pain, it is a challenging condition that significantly impacts the patient's quality of life, particularly in chronic skin diseases¹. Treatment is primarily aetiological^{2,3}, but usual treatments are not always totally efficient in relieving pruritus. In several cases, the aetiological diagnosis is unknown, and the treatment of the cause is not possible. Therefore, symptomatic treatments are useful.

The benefit of music interventions has been demonstrated in various conditions, such as anxiety⁴, autistic spectrum disorders⁵, depression⁶, dementia⁷ and largely in pain. Indeed, while the effect of music intervention has been demonstrated to treat pain in a high number of studies analysed in meta-analyses^{8,9,10,11}, there are very few data concerning its effect on pruritus.

From a pathophysiological point of view, pruritus has many clinical similarities with pain, as well as differences. Both pruritoception and nociception are physiological sensations prompting the avoidance of the sensation-causing stimulus. Along with the inherent discomfort associated with itch and pain, both induce protective behaviours (scratching and withdrawal behaviour, relief by heat or cold, respectively) in an attempt to reduce one's exposure to potential adverse outcomes¹². Some similarities between pruritus and pain physiopathology could be a lead in understanding the mechanism of action. Itch is encoded by distinguishable neurons both in the peripheral and the central nervous system (CNS)¹³. However, itch also interacts with the other sensory modalities at multiple locations, from its initiation in a particular dermatome to its transmission to the brain where it is finally perceived. Itch is transmitted predominately by unmyelinated, slow-conducting C-fibres that extend to the dermo-epidermal junction with free endings penetrating into the epidermis where sensation is detected. The cell bodies for these fibres are in the dorsal root ganglia, just outside the spinal cord, then follow the classic pathways through a first neuron, then the dorsal horn of the spinal cord and then a second neuron. At this point, both itching and pain involve secondary transmission neurons that ascend via the contralateral spinothalamic tract to the thalamus. At the cerebral level, there is no single centre of pruritus but several motor and sensory areas involved. The final perception may be modulated (inhibited or enhanced) by various factors. Like pain, itch perception can be diminished by non-invasive treatments through interactions between different cerebral areas¹⁴. Consequently,

similarities between itch and pain suggest that music may have an interest in the management of chronic pruritus, especially since conventional treatments have only partial effectiveness in some skin diseases.

The objective of this randomized controlled trial was to evaluate the effectiveness of a music intervention on the intensity of pruritus in patients with skin diseases by comparing the intervention with the application of an emollient.

PATIENTS AND METHODS

This randomized, controlled, comparative, single-centre study was conducted in the dermatology department of the University Hospital of Brest. The trial was registered on ClinicalTrials.gov with the title 'Study Evaluating the Benefit of Music Therapy on Pruritus in Patients with Pruritic Skin diseases (PRURI-MUSIC)' and the identifier NCT 03701971. The study protocol was approved by the institutional ethics committee (Comité de Protection des Personnes Ouest III, Brest, France).

Patients

Patients were recruited in the dermatology department of the University Hospital of Brest. Inclusion criteria were inpatients with a pruriginous chronic skin disease (such as psoriasis, atopic dermatitis, urticaria), a length of the disease greater than one month, a pruritus intensity greater than or equal to 3 on 10 on the Numerical Rating Scale (NRS) and age ≥ 18 years old. Non-inclusion criteria were age < 18 years old, major hearing impairment, cognitive disorder, pregnancy or lactation, refusal to participate, life-threatening condition, non-affiliation to a National Health Insurance system and a lack of legally competency. Written consent was obtained from all patients.

Interventions

The patients were randomized into 2 groups (ratio 1:1): music intervention (experimental group) or emollient (control group). Among the 53 patients to whom the study was proposed in total, only three patients refused to participate due to a lack of interest in music. Once the consent form was signed, demographic and clinical data were collected. Skin and psychiatric diagnoses, as

well as usual medication were reported by clinical investigator which performed anamnesis and clinical examination. Then, they responded to different questionnaires before intervention:

- Pruritus intensity on the NRS (from 0 to 10).
- The 5D itch scale questionnaire is a brief but multidimensional questionnaire designed to be useful as an outcome measure in clinical trials. This scale presents 5 points to clarify the characteristics of pruritus (degree, duration, direction, disability and distribution)¹⁵. The final 5D scoring ranges from 5 (no pruritus) to 25 (most severe pruritus)
- The ItchyQoL scale (Itchy Quality of Life): this questionnaire measures the quality of life in patients with chronic pruritus. It is composed of 22 items regarding symptoms, functions, emotions and self-perception¹⁶. Each of the questions is scored 1–5 (1: never; 2: rarely; 3: sometimes; 4: often; 5: all of the time) and score is ranging from 22 to 110.
- The State-Trait Anxiety Inventory Questionnaire (STAI-Y A). It is a self-assessment validated questionnaire consisting of 20 propositions. Each proposition has a score ranging from 1 to 4, with 1 indicating the lowest level of anxiety and 4 the highest level^{17,18}. The scores can be classified into five levels: greater than 65 (very high), 56 to 65 (high), 46 to 55 (moderate), 36 to 45 (low), and less than 35 (very low).

Music intervention

The individual receptive music method was used. The music was chosen based on the patients' personal taste from a selection of various styles on a tablet. A single individual music session was held at the beginning of the patient's hospitalization. The music was broadcasted with headphones, with an ocular mask while lying down, in a quiet room. The standard music sequence, lasting 20 minutes, was broken down into several phases, which gradually brought the patient into a state of relaxation according to the 'U sequence' method ¹⁹. The assembly in U involves a gradual reduction of the musical rhythm, orchestral training, frequencies and volume (descending U-phase). After a phase of maximum relaxation (bottom part of the U), a re-enlivening phase follows (ascending 'U' segment) (Fig. 1). All of the music sequences, constructed using the 'U sequence' method, were recorded by the company Music Care (Paris, France).

Place to insert Figure 1

Control group

The control group received an application of an emollient cream on the entire body (Cold Cream Gilbert, Hérouville-Saint Clair, France).

One hour after the intervention, the patient answered the following:

- The pruritus NRS.
- The STAI-Y A questionnaire.
- The Patient's Global Impression of Change (PGIC). This is a self-report measure that reflects a patient's belief about the efficacy of a treatment. It is composed of a 7-point scale depicting a patient's rating of overall improvement²⁰.

Outcomes

The primary outcome was the evolution of the pruritus NRS between the beginning and one hour after the procedure. The secondary outcomes were the effect on patient anxiety (STAI-Y A scale), the impact on quality of life (ItchyQoI), and patient satisfaction, as evaluated with the PGIC questionnaire.

Sample size

An improvement on the pruritus NRS scale of 1 point in the control group and of 3 points in the experimental group, i.e. a 2-point difference between groups, was anticipated. Assuming this difference, a 5% type I error (two-sided), a power of 90% and a standard deviation of 2, the required number of subjects was estimated at 23 per group. To anticipate any withdrawal of consent, the sample size was increased to 25 subjects per group.

Concomitant medication

Patients' usual treatments that could potentially modify the results of the study (oral or topical anti-pruritic drugs, analgesics, psychotropic treatments, other aetiological treatments of dermatoses, etc.) were noted. Patients were not authorized to use or apply the treatments from at least 6 hours before and during the protocol in both groups to avoid interference with the tested intervention.

No modifications or significant changes in patient medication were observed during the study.

Conventional treatment usually proposed during hospitalization was set up right at the end of the study.

Randomization

The patients were randomized using a computer-generated list of random numbers through a dedicated website.

Statistical analysis

All randomized patients were analyzed (intent-to-treat principle). Quantitative data were described in terms of sample size, mean, standard deviation and range (minimum and maximum). Qualitative data were described by their distribution in terms of sample size and percentage by class. The mean difference before and after the intervention regarding pruritus intensity was evaluated in each group and compared using the Student's t test (or a non-parametric Wilcoxon test). The percentage improvement in the pruritus NRS was assessed in the same way. Qualitative variables were compared with the chi-squared test or Fisher's exact test. The statistical analysis was carried out in collaboration with the Department of Clinical Research and Innovation of the University Hospital of Brest and was performed using SAS software V9.4.1.

RESULTS

Place to insert Figure 2

The study took place from November 2018 to May 2019. Fifty patients were included, 25 in each group (Fig. 2). Demographic data are presented in table 1. Sixty-two percent of patients were male, with an average age of 60.7 years. The most common skin diseases were psoriasis (N=10), atopic dermatitis (N=8) and contact eczema (N=6). Eighty-six percent of patients had pruritus daily, and 42% had permanent itching. Forty-four percent of patients had itching for less than 6 months, 10% for 6 to 12 months, 20% for 1 to 5 years and the rest for more than 5 years.

Place to insert Table 1

Concerning the primary endpoint, the intensity of pruritus decreased more significantly for patients in the music intervention group than for patients in the emollient group : 2.3 (SD 2.1) (95% CI: [1.4; 3.1]) and 1.2 (SD 1.7) (95% CI: [0.5; 1.9]) (table 2), respectively. A statistically

significant differential decrease of 1.1 points (95% CI: [-0.01; -2.2]) was observed between both groups ($p=0.047$).

Place to insert Table 2

The STAI-Y A score before intervention was 44.6 (SD 13.9) (95% CI: [38.9; 50.3]) in the control group and 48.3 (SD 11.0) (95% CI: [43.7; 52.9]) in the experimental group. No statistically significant differences were observed before intervention (-3.7; 95% CI: [-10.8; 3.5]; $p=0.3$). There was a decrease in anxiety in both groups: a decrease of 6.5 (SD 11.2) (95% CI: [1.9; 11.1]) in the experimental group and 4.0 (SD 8.9) (95% CI: [0.3; 7.7]) in the control group. However, the difference of -2.5 points (95% CI: [-8.2; 3.3]) between both groups was not statistically significant ($p=0.4$).

Figure 3 represents the percentage of patients by the degree of anxiety intensity before and after the intervention in the experimental group.

Place to insert Figure 3

Among patients who received the music intervention, 64% reported feeling an improvement, 91% would recommend the music intervention and 64% would like to continue this practice. There was no significant difference between the two groups regarding satisfaction questionnaires.

A minor anxiety attack was observed at the end of the music intervention for one patient in the experimental group, which did not result in the session being stopped and was resolved with the use of an anxiolytic.

DISCUSSION

To the best of our knowledge, our study is the first randomized control trial evaluating the effect of a music intervention on pruritus as a primary endpoint. Because of the music intervention, the intensity of pruritus decreased by 2.3 on a scale of 10, and the patient satisfaction was high. The average ItchyQol score was 64.8/110, showing a significant impact on the quality of life of pruritus. The majority of patients who were offered to participate accepted the music intervention (3 refusals upon 53 proposals), demonstrating the feasibility and the global interest for this method. Music sessions were reproducible using the U-shaped technique, and the

different music styles were adapted for the varying tastes of patients. Despite a large choice of musical styles, the three-phase composition of all the sequences ("stimulating", "relaxing" and "awakening") enables its standardized use by healthcare professionals and in clinical trials. The superiority of the "U" assembly technique over standard relaxation music in the treatment of pain was demonstrated by a randomized controlled study using the Music Care® software¹⁰.

Only one study was previously published evaluating the effects of a music intervention on pruritus. One hundred and fourteen patients undergoing haemodialysis were randomized into a control group (n = 57) or an experimental group (n = 57) who received 30 minutes of live saxophone music. Blood pressure, pulse rate, glycaemia, oxygen saturation, pain, mood and itching levels were measured before and after the live music performance. An improvement was observed regarding all studied parameters. Patients receiving the music intervention had a decrease in pruritus intensity (a secondary endpoint) of 75.7%²¹.

Like for pain²², the impact of music on pruritus is probably multi-factorial, with psychological, cognitive, and affective mechanisms. One possible hypothesis could be that diverting attention and relaxation may account for the decrease in itch sensations, similar to the effect of distraction that is observed in pain. However, among the main mechanisms assumed, distraction and relaxation are not sufficient to explain this effect. Because of the absence of positive emotions, anxiety could inhibit pain²³ or itch. In our study, anxiety levels were reduced but not significantly. A study of individuals subjected to tonic nociceptive stimulation showed specific neural activation induced by listening to music, testifying of the involvement of inhibitory descending pathways²⁴. Indeed, music modulated pain responses in the brain, brain stem, and spinal cord, with changes in neural activity that are consistent with the engagement of the descending analgesia system.

Because peripheral sensitization and loss of descending inhibition are hallmarks of chronic pruritus²⁵, it can be assumed that music could also work by activating inhibitory neural circuits.

Our study has some limitations. The effectiveness of music was observed on a single session, and the NRS was measured only once, one hour after the intervention in our study. This does not allow us to conclude that it is effective in a long-term perspective. We decided to conduct our study on a group of hospitalized patients to ensure that patients would receive music in good conditions and with good reproducibility. The effect was measured in a single session at the

hospital to avoid the confounding effect of other treatments. In a large majority of pruriginous skin diseases, the use of emollient is considered to be efficient and is often proposed in primary or adjuvant approaches²⁶. However, the anti-pruriginous effect of emollient has been little studied. We chose the use of emollient as a comparator. Both interventions showed a benefit in our study, and it can be assumed that combining them could lead to better patient improvement.

The repeated use of music interventions over the long term has to be evaluated in further studies. Now that a benefit has been demonstrated in a hospital setting, it could be adapted and tested at home.

CONCLUSION

Chronic pruritus management is complex. The use of music using the "U"-shaped technique is a simple non-pharmacological method that can be a tool in the management of chronic pruritus, in addition to other aetiological or symptomatic treatments.

Tables

Table 1: Individual characteristics of the patients at the time of inclusion

		Total (N=50)	Control Group (N=25)	Experimental Group (N=25)
Sex, n (%)	Male	31 (62)	13 (52)	18 (72)
	Female	19 (38)	12 (48)	7 (28)
Age	Mean (SD)	60.7 (20.2)	57.5 (22.9)	63.9 (16.9)
	Min-Max	20-93	20-93	24-89
Clinical Data				
Skin diseases, n (%)	Psoriasis	10 (20)	7 (28)	3 (12)
	Atopic dermatitis	8 (16)	4 (16)	4 (16)
	Contact eczema	6 (12)	2 (8)	4 (16)
	Cutaneous lymphoma	0 (0)	0 (0)	0 (0)
	Drug-induced dermatitis	1 (2)	1 (4)	0 (0)
	Lichen	0 (0)	0 (0)	0 (0)
	Pruritus <i>sine materia</i>	2 (4)	2 (8)	0 (0)
	Prurigo nodular	4 (8)	1 (4)	3 (12)
	Bullous pemphigoid	2 (4)	1 (4)	1 (4)
	Unknown	17 (34)	7 (28)	10 (40)
Itch duration (years)	Mean (SD)	9.9 (16.4)	7.9 (12.1)	11.9 (19.9)
Usual aetiological treatment, n (%)	Topical steroid	21 (42)	10 (40)	11 (44)
	Emollient	22 (44)	12 (48)	10 (40)
	Antihistaminic	7 (14)	3 (12)	4 (16)

		Total (N=50)	Control Group (N=25)	Experimental Group (N=25)
Psychotropic medication, n (%)	Antidepressant therapy	7 (14)	3 (12)	4 (16)
	Sedative or hypnotic therapy	6 (12)	2 (8)	4 (16)
	Anxiolytic treatment	11 (22)	5 (20)	6 (24)
	Pain treatment	16 (32)	10 (40)	6 (24)
Psychiatric history, n (%)	Depression	10 (20)	4 (16)	6 (24)
	Anxiety	15 (30)	7 (28)	8 (32)
	Psychotic disorder	0 (0)	0 (0)	0 (0)
	Sleeping disorder	17 (34)	9 (36)	8 (32)
Patient's Quality of Life				
ItchyQoL score	Mean (SD)	64.8 (17.8)	62.9 (19.7)	66.7 (15.9)
	Min-Max	29-102	29-100	34-102
5D Itch Scale				
5D itch scale score	Mean (SD)	17.9 (3.5)	17.6 (3.5)	18.3 (3.5)
	Min-Max	9-24	9-23	12-24

Table 2: Analysis of the primary endpoint

Variable		Total (N=50)	Control group (N=25)	Experimental group (N=25)	p*
Pruritus NRS before	Mean (SD)	6.0 (2.2)	5.7 (2.3)	6.3 (2.1)	0.3

Variable		Total (N=50)	Control group (N=25)	Experimental group (N=25)	p*
intervention	Min-Max	3-10	3-10	3-10	
Difference in NRS before - after	Mean (SD)	1.7 (1.9)	1.2 (1.7)	2.3 (2.1)	0.047
% of improvement after intervention**	Mean (SD)	27.8 (29.7)	21.2 (27.4)	34.4 (31.0)	0.1

*Student's *t* test or Mann-Whitney/Wilcoxon test

$$** \frac{\sum_{i=1}^n (NRS\ Before_i - NRS\ After_i) / NRS\ Before_i}{n}$$

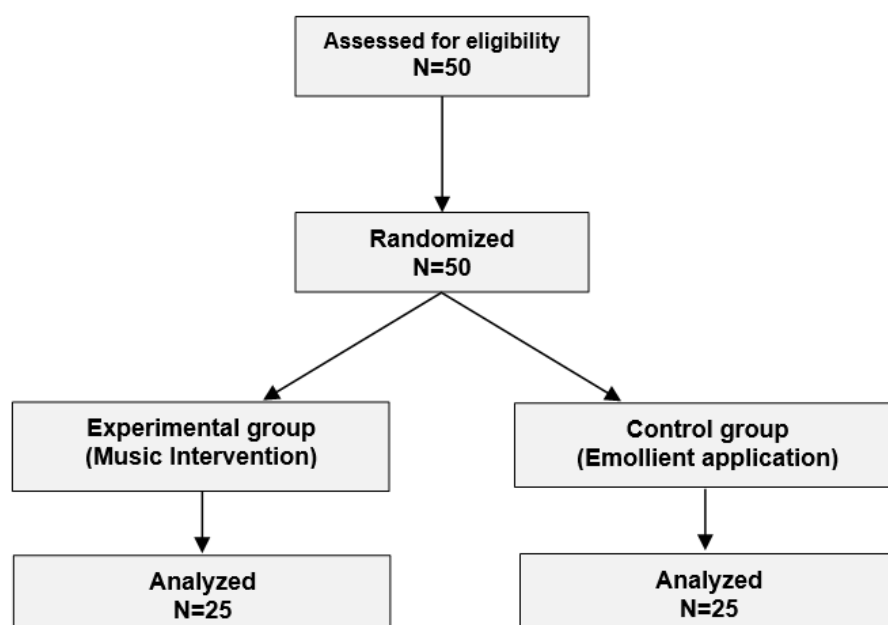
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Figure 1. The “U sequence”

Figure 2. The flow chart

Figure 3. The percentage of patients by degree of anxiety intensity before and after the intervention in the experimental group

Figure 2. The flow chart



ACKNOWLEDGEMENTS

We acknowledge all participants in the study, Dr Guétin Stéphane from the Music Care Company for delivering the Music Care® software and the equipment to complete the musical interventions, and the Delegation of Clinical Research and Innovation of the CHRU of Brest for its participation in the study.

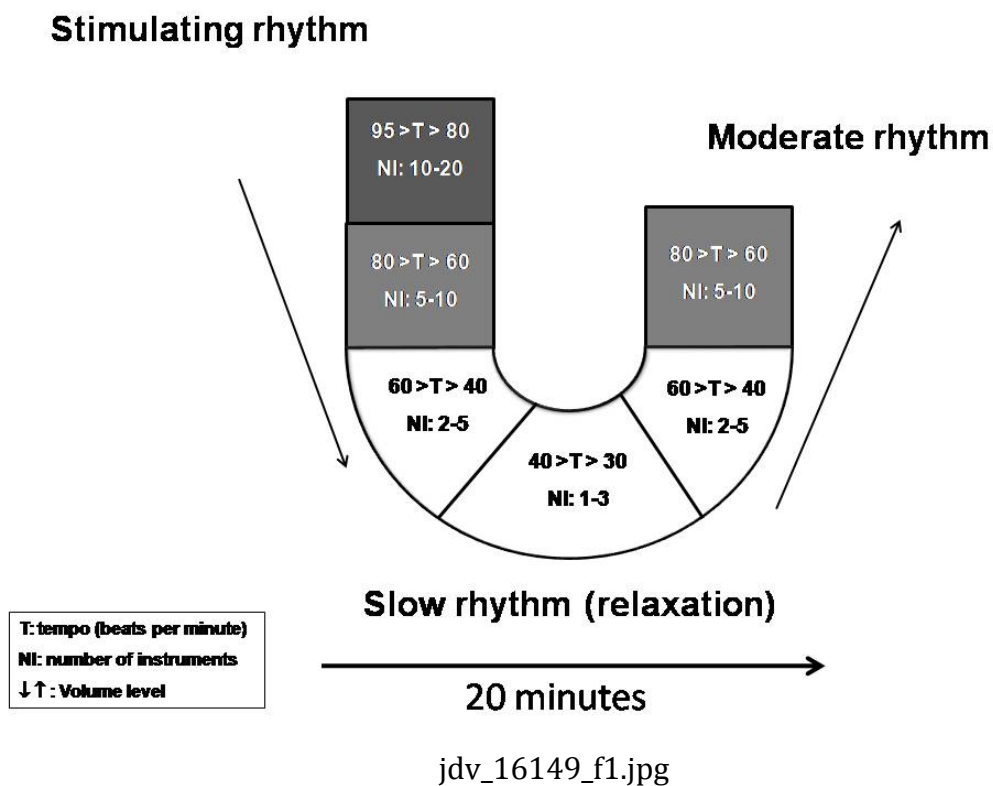
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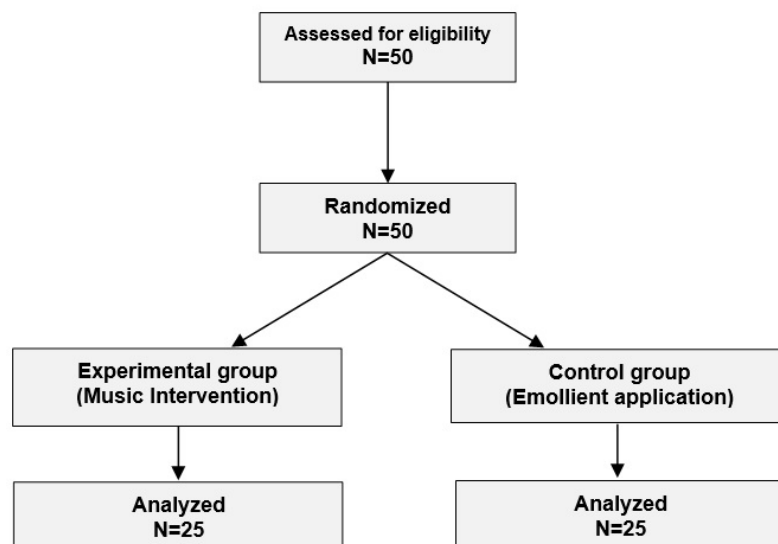
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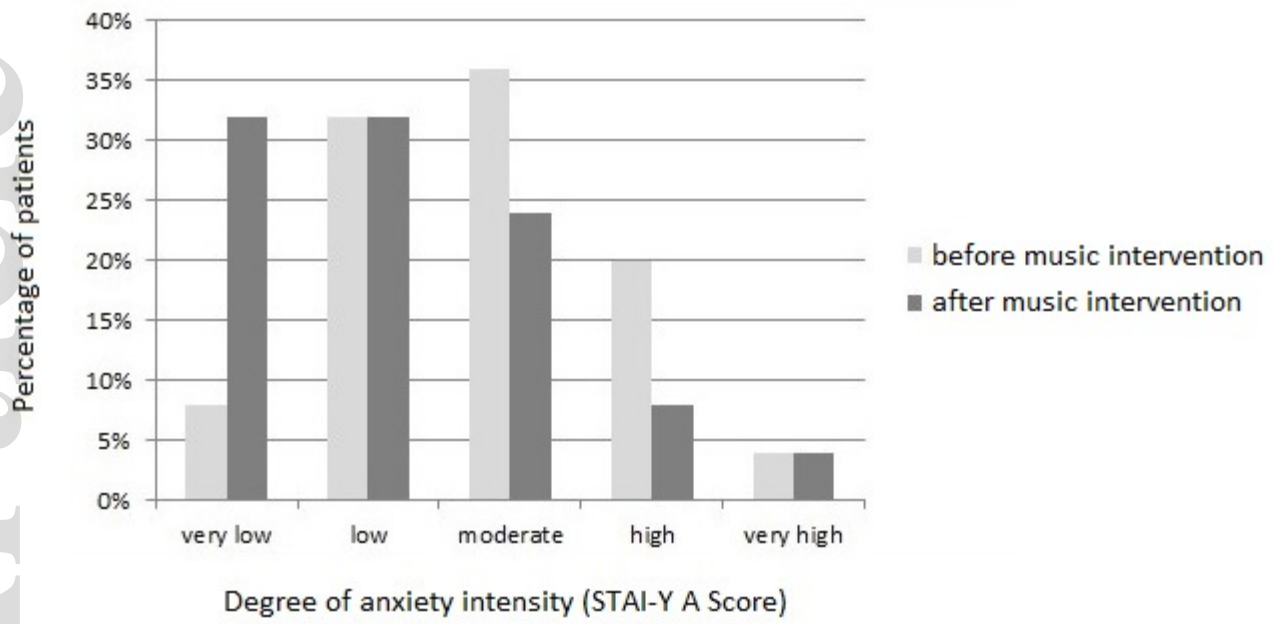
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