



# Music and biological stress dampening in mechanically-ventilated patients at the intensive care unit ward—a prospective interventional randomized crossover trial<sup>☆,☆☆</sup>

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Music;  
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## Abstract

**Purpose:** To evaluate the impact of slow-tempo music listening periods in mechanically ventilated intensive care unit patients.

**Methods:** A randomized crossover study was performed in a 16-bed, adult critical care unit at a tertiary care hospital. Still-sedated patients, mandating at least 3 more days of mechanical ventilation, were included. The intervention consisted in two 1-hour daily periods of music-vs-sham-MP3 listening which were performed on Day 1 or 3 post-inclusion, with a Day 2 wash-out. “Before-after” collection of vital signs, recording of daily sedative drug consumption and measurement of stress and inflammatory blood markers were performed.

**Results:** Of 55 randomized patients, 49 were included in the final analyses. Along with music listening, (i) vital signs did not consistently change, whereas narcotic consumption tended to decrease to a similar sedation ( $P = .06$  vs sham-MP3); (ii) cortisol and prolactin blood concentrations decreased, whereas Adreno Cortico Trophic Hormone (ACTH)/cortisol ratio increased ( $P = .02$ ;  $P = .038$ ; and  $P = .015$  vs sham-MP3, respectively), (iii) cortisol responders exhibited reversed associated changes in blood methionine (MET)-enkephalin content ( $P = .01$ ).

**Conclusions:** In the present trial, music listening is a more sensitive stress-reliever in terms of biological vs clinical response. The hypothalamus-pituitary adrenal axis stress axis is a quick sensor of music listening in responding mechanically ventilated intensive care unit patients, through a rapid reduction in blood cortisol.

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## 1. Introduction

Music listening is being increasingly widely used for stress release in all areas of medicine, including oncology, geriatrics, gastroenterology, cardiology, anesthesiology, surgery, pediatrics, palliative care, psychiatry, and intensive care [1]. Indeed, there have been historical references of its

benefits, with both Kings Saul and George commissioning harp playing to reduce their stress. Music listening is known to influence both frontotemporal cortical areas and the limbic system, and causes psychophysiological responses [2,3]. It is involved in specific brain functions such as memory and emotional state and thus can bring a state of relaxation, improve temper and increase motivation [4]. More specifically, listening to relaxing or stress-releasing music can also increase the release of endorphins and enkephalins, and decrease circulating catecholamines [4,5]. Stress-releasing music is often slow-tempo (60 bpm of rhythm) to which heart and respiratory rates can also be synchronized [4]. The potential benefits are a reduction in pain and a lowering of blood pressure, heart rate, oxygen consumption, muscle tension, and activity of sweat glands [1,4]. Intensive care units (ICU) are a stressful milieu, and mechanical ventilation (MV) is potentially painful and uncomfortable. In this context, an appropriate and titrated pharmacological support is almost always mandatory to provide comfort without oversedation. While sedative medications are cornerstone in this goal, the way the latter should be administered (intermittent vs continuous with daily interruption) remains controversial [6-8]. In addition, these drugs are expensive, can lengthen the duration of MV, and have potentially lethal side-effects as well as worsen outcome.

Most studies using music in MV patients tended to show a beneficial effect on clinical physiological parameters such as pulse and respiratory rate, anxiety and pain as well as blood pressure [9]. Of note, Conrad et al observed a reduction of sedative drug consumption in a small cohort of MV patients listening to an hour of a Mozart's piano sonata [5]. On a biological standpoint, they also demonstrated that blood interleukin-6 (IL-6), a cytokine involved in early inflammatory processes, as well as dehydroepiandrosterone, an upstream common precursor of steroids, were decreased whereas growth hormone was increased in response to listening to this classical music [1,5]. Additional evidence that music listening probably affects the hypothalamus-pituitary-adrenal (HPA) axis also stems from the work of Chlan et al who evaluated blood levels of cortisol and corticotrophin in another small cohort of MV patients [10].

However, for the time being, (i) only a limited number of MV-patients have been tested with music listening, (ii) the impact of music has never been evaluated in a crossover design where patients are their own controls, (iii) patients still maintained on mild sedation instead of those with discontinued sedation; have not been thoroughly studied for responsiveness, and (iv) several essential short-releasing biological stress/inflammatory responses have not been explored. In light of these observations, we postulated that slow-tempo music listening during MV in ICU patients can (1) reduce sedative drug consumption and slow down vital signs in not fully alert patients and (2) dampen inflammatory and HPA axis hormonal release.

## 2. Materials and methods

### 2.1. Study design and population

This prospective randomized-controlled crossover trial included patients requiring invasive mechanical ventilation, while taking benefit of patients being their own controls. The trial received the approval of our local ethical review board (Comité d'Éthique de la Recherche en Santé chez l'Humain du CHUS), and a written informed consent was obtained from the patient's relatives with subsequent approval of randomized patients when possible. This trial was registered in the ClinicalTrials.gov protocol registration system under NCT00880035. The inclusion criteria were the following:

- 1- Adult patients 18 years or older;
- 2- Requiring sedation medication for a Sedation-Agitation Scale (SAS) 3 or 4;
- 3- Necessitating at least 3 more days of invasive MV, but on a self-triggering mode (as daily assessed/estimated by the on-duty medical intensive care unit [MICU] staff);
- 4- Stabilized overall medical condition (ie, acute disorder(s) resolved or under control, and sedation tapering and MV weaning modes initiated).

Patients were excluded from the protocol if they were deaf; as they would not be able to listen to music, or pregnant, needing a SAS 1 or 2 or neuromuscular blockade. All patients were screened and recruited at the CHUS MICU of Fleurimont which is a 16-bed mixed medical-coronary unit for adult patients with an average annual admission rate of approximately 1000/year. The trial was conducted from Jan 2009 to April 2011 and 720 patients were maintained at least 1 day on invasive MV during this period.

A computer-generated block randomization list was prepared by the investigators. Randomization was concealed using numbered, opaque sealed envelopes and was revealed by an ICU staff member not involved in the direct care of the randomized patient. This staff member took a first blood sample and recorded baseline vital signs (VS) as well as sedative infusion rates (step 1); positioned the music system (ie, MP3) on the patient's head and started the listening period (step 2); and repeated step 1 procedures at the end of the listening period (step 3). All efforts were made to avoid any nonurgent interventions from steps 1 to 3.

#### 2.1.1. Steps 1 and 3

VS (arterial blood pressure, heart rate, respiratory rhythm) were monitored and validated every day of the protocol, although all data recorded for the final analysis were those obtained immediately before and at the end of the MP3 (music or sham) listening periods on both AM and PM sessions (ie, at steps 1 and 3) for a one-to-one value comparison. In this ICU and during the trial period, sedative drugs were generally administered intermittently or titrated

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