

# Some effects of sound and music on organisms and cells: a review

Exbrayat Jean-Marie<sup>1\*</sup>, Brun Claire<sup>1</sup>

<sup>1</sup>UMRS 449 "General Biology – Reproduction and Comparative Development" Lyon Catholic University (UCLy – UDL), Ecole Pratique des Hautes Etudes (EPHE, PSL), 10 place des Archives, 69288 Lyon Cedex 02, France.

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## ABSTRACT

In animals, the sound vibrations are captured by the auditory cells, then transformed into electrical signals and conveyed to the nervous centers where they can be interpreted such as music. A lot of studies concern the effect of sound on the auditory cells and on the brain. Nevertheless, musical vibrations also affect other cells types in several organisms. These researches being not of the same nature, they need to be classified in order to provide elements of understanding the effects of music on cell biology. A lot of works were done on the effects of music on non-auditory cells. Effects on growth, apoptosis, immune system, protein activities in animal, plant and bacterial cells have been shown. These effects are of a physiological nature and require molecules and physicochemical mechanisms. Some works were performed on vegetal or animal total organisms, others directly on cells themselves, using cell cultures. Few works concern eukaryotic unicellular organisms. Results of these studies show music and sound exert effects on the physiology. But the experiments and results are still well disparate, with effects of different types of music on organisms via auditory on non-auditory cells, sometimes involving both auditory and non-auditory cells. Whatever the large variation of results, the study of the effects of sound and especially music on the cells is a subject on the future, considering the immense possibilities offered by music in modulating physiology, with potential therapeutic applications.

*Keywords: Sound, music, auditory cell, non-auditory cell, plant, animal, unicellular organism.*

## 1. INTRODUCTION

The music is an organized sequence of sounds. In animals, the sound vibrations are captured by the auditory cells where they are transformed into electrical signals, themselves conveyed to the higher nervous centers [1]. At this level, the information is interpreted and reconstructed to give music with a particular emotional connotation [2-4]. Since several years, the effects of music have been studied on several disparate ways, from the decrease of stress in different kinds of patients to the effects on several biochemical factors. For example, music reduced anxiety in women undergoing colposcopy. The authors of the study concluded it was possible the experiment increased the knowledge levels, and the clinical consent to the colposcopy was more easily obtained [5]. In a totally different register, the effects of music are beneficial on emotions, stress, and also immune system. Biochemical molecules such as neurotransmitters, hormones, cytokines, and peptides act such as intermediary between music and its effects [6].

\* E-mail address: [jmexbrayat@univ-catholyon.fr](mailto:jmexbrayat@univ-catholyon.fr); [jean-marie.exbrayat@ephe.psl.eu](mailto:jean-marie.exbrayat@ephe.psl.eu)

32 Among the studies, a lot of them concern the effect of sound wavelengths on the auditory  
33 cells. Nevertheless, musical vibrations also affect other cells types, and not only on animal  
34 organisms. Since several years, researchers have studied the effects of music on different  
35 aspects of physiology in several kinds of organisms. This review aims to take a quick look at  
36 these works, which are still disparate, and to classify these researches being not of the same  
37 nature, to provide elements of understanding the effects of music on cell biology. Firstly, the  
38 main effects of sound and more especially music in plants and unicellular prokaryotic and  
39 eukaryotic organisms will be described. Then, the effects of music will be examined  
40 successively on different aspects of animal biology on the total organism, and also on  
41 isolated cells and cell cultures. Some aspects of harmful effects of noise on organisms will  
42 be also given.

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## 44 **2. THE EFFECTS OF SOUND AND MUSIC UPON NON-ANIMAL ORGANISMS**

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### 46 **2.1 On plants**

47

48 Plant cells respond to sound waves. These can influence germination rates and increase  
49 plant growth and development, improving the yield of some crops [7,8]. In addition, it is  
50 currently accepted that sound waves can enhance the plant immunity against pathogens [9]  
51 and may also increase their tolerance to drought [10]. More surprisingly, plants can  
52 recognize the mating sounds of insect larvae and the buzz of a pollinating bee and respond  
53 accordingly [11]. Thus, evidence of acoustic communication during plant-animal interactions  
54 seems to be confirmed [12]. For example, some bat-dependent plants have adapted to their  
55 echolocation systems by providing acoustic reflectors to attract their animal partners [8].

56

57 At the cellular level, sound vibrations can affect microfilament rearrangements, increase  
58 levels of soluble polyamines and sugars, modify the activity of various proteins, and regulate  
59 the transcription of certain genes [7,13,14]. In Chinese cabbage and cucumber exposed to  
60 ultrasound, to classical music or loud sounds, the level of polyamines and the following  
61 oxygen uptake increased significantly [13]. The increases observed are greater in the plants  
62 exposed to musical sounds. On the other hand, the authors did not observe a variation of the  
63 vitamin C level. The effects of the sound are complex, and influence the physiological  
64 mechanisms. In particular, acoustic stress as environmental stress induces a downregulation  
65 of the expression of certain genes [14].

66

### 67 **2.2 Effects on unicellular organisms**

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69 Unicellular cells, eukaryotic or prokaryotic, are sensitive to the effects of music which can  
70 affect survival and activity of microorganisms [15]. In *Escherichia coli*, audible sound  
71 increases the colony forming under the normal condition, and enhance the inhibitory effect of  
72 osmotic stress [16]. Indian music with sounds between 38 and 689 Hz had a positive effect  
73 on the growth of bacteria and yeasts (with an increase of 3.15 to 40.37%), except for the  
74 species *Serratia marcescens*. Music also influences the production of metabolites, antibiotic  
75 sensitivity. The bacterium *Chromobacterium violaceum* and the yeast *S. marcescens* break  
76 down more quickly cephazoline, an antibacterial agent. In organisms subject to musical  
77 vibrations, membrane permeability seems to be impaired; the intracellular concentration of  
78 calcium and potassium and the protein content are also significantly different from those of  
79 the control. The "audible sound in the form of music" like said the authors, has thus been  
80 able to affect the growth, metabolism and antibiotic sensitivity of bacteria (prokaryotes) and  
81 yeast (eukaryotes) [17]. In *Staphylococcus aureus*, low-intensity pulsed waves decreased  
82 the number of bacteria colonies compared to bacteria which were not submitted to sound.  
83 The cell membranes of the tested bacteria were partially broken and the thickness of  
84 bacterial cell wall was higher in the bacteria submitted to sound (41.54 nm instead 24.27 nm)

85 [18]. Experiments in several bacteria, and particularly *Bacillus subtilis* and *B. carboniphilus*  
86 suggested sound communication between bacteria [19,20]

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### 88 3. THE EFFECTS ON ANIMALS

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#### 90 3.1. Reception of sounds by auditory cells

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92 Hearing cells, still called hair cells, are sensory cells emitting stereocilia. These cells are  
93 arranged along the basilar membrane lining the inside of the cochlea, the spiral hearing  
94 organ. The outer cylindrical cells contract periodically by amplifying the sound signal, and the  
95 inner pear-shaped hair cells transform the amplified signal into an electrical signal [21,22].

96 The cells situated at the beginning of the cochlea receive the highest frequencies; those at  
97 the end of the spiral receive the lowest ones. The deflection of stereocilia causes the  
98 opening of ion channels, causing the entry of  $K^+$  ions which depolarize the cell and create an  
99 electrical receptor potential. Calcium channels are opened depending on the potential of the  
100 receptor and  $Ca^{++}$  enter the cell, releasing glutamate, a neurotransmitter, at the base of the  
101 cell at the level of synaptic ribbons, related to the axons of neurons. Glutamate binds to  
102 afferent nerve fiber receptors and triggers action potentials in the nerve. To resume, the  
103 inner hair cells are set in motion by a sound wave that triggers the release of  
104 neurotransmitters, creating a signal that is transmitted to the auditory areas of the brain [23-  
105 26].

106

107 Non-auditory cells can also respond to sound. The fluids contained by all the cells are thus  
108 sensitive to the variations of pressure induced by the sound waves and no cell type can  
109 theoretically hinder a pure sound or music. Several studies show that the mechanisms of  
110 growth arrest and cell death induced by acoustic vibrations are similar for auditory and non-  
111 auditory cells [27,28].

112

#### 113 3.2. Some effects on the whole organisms

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##### 115 3.2.1. Effects on stress

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117 The effects of music on stress have been well investigated, and several reviews were  
118 published [29,30]. These studies are managed in different manners that can be illustrated  
119 with two examples, one concerning human beings, the other concerning animals.

120

121 Listening to music is used since a long time in order to induce relaxation. The mechanisms  
122 of these beneficial effects have been studied in persons listening music. After listening  
123 music, the number of blood mononuclear cells and morphine 6 glucuronide increased; IL-6  
124 levels decreased significantly, IL-1b, IL-10 and cortisol did not vary. In people having listen  
125 music, the signal molecule changed in plasma, and was accompanied with some  
126 physiological changes [31].

127

128 The effects of auditory and physical enrichment have been studied in chicks. For auditory  
129 enrichment, the chicks have been submitted to classical music. For physical enrichment,  
130 others chicks have been bred in front of hanging colored string bunches and with barley  
131 grains on the floor. Music reduced the stress characterized by the measure of different  
132 parameters (duration of tonic immobility, white blood cells of birds / lymphocyte ratio, and  
133 fluctuating asymmetry). The results suggested that auditory enrichment from classical music  
134 reduced stress in chicks. At contrary, no significant results were obtained with physical  
135 enrichment [32].

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##### 136 3.2.2. Some effects on embryonic development

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138 The fluctuating asymmetry of an organism is a small random deviation from a perfect  
139 bilateral symmetry that results from genetic and / or environmental stress during  
140 development [33]. During growth, morphological differences were found in chicks reared  
141 without music compared to chicks with a musical environment: asymmetry of wing length,  
142 leg thickness and greater combined asymmetry. Like see above, the auditory enrichment  
143 decreased the fluctuating asymmetry in chicks [32].  
144

145 Several studies have shown some effects of music on the embryonic development of brain.  
146 Music facilitates the neurogenesis, regeneration and repair of neurons in humans [34]. In  
147 rats, the exposure to music during pregnancy increased the neurogenesis in the  
148 hippocampus and enhanced spatial learning ability. But inversely, the exposure to noise  
149 (which can be defined such as an unorganized sequence of frequencies) during pregnancy  
150 decreased neurogenesis in the hippocampus, with growth retardation, and impaired spatial  
151 learning ability [35].  
152

153 In brain of music-overstimulated developing chicks, an increase of auditory nuclei was  
154 observed consequently to the increase in number and size of neurons. In animals submitted  
155 to attenuated sound, the number of cell nuclei of large size slightly increased, and the  
156 number of glial cells also increased. The dissociated responses of neurons and glial cells  
157 suggested these two kinds of cells were independently regulated [36]. Prenatal auditory  
158 enrichment of chicks with species-specific sounds or with other music modulates the  
159 expression of *Bcl-2* and *Bax* and consequently the programmed cell death [37]. Apoptosis is  
160 indeed a fundamental phenomenon in shaping the future nervous system in vertebrates [38].  
161 Postnatal auditory stimulation influences early perceptual learning. The effects of several  
162 kinds of sound, music (KV 448, Mozart), and silence was studied on adult neurogenesis in  
163 mouse. After 24h of exposition to all these stimuli, including silence, the proliferation of  
164 precursor cells labeled with BrdU increased. But after 7 days of exposure, only silence  
165 increased the number of labeled neurons [39].  
166

167 In chicks, some works showed that prenatal auditory stimulation was associated with  
168 morphological and biochemical variations in the hippocampus and brainstem auditory nuclei.  
169 Consequences were observed upon the ability for spatial orientation and learning of chicks.  
170 High decibel (110 dB) music stimulation increased moderately noradrenaline level in plasma  
171 and consequently positively modulated spatial orientation, learning and memory in one-day-  
172 old chicks. Noise increased plasma noradrenaline level and impaired the spatial behavior. In  
173 music-stimulated chicks, two markers of synaptogenesis, synaptophysin and PSD-95,  
174 significantly increased [40]. In animals stimulated by music, increase of neuron number and  
175 neuronal nuclear area was observed using histology and image analysis [41]. A reduction of  
176 total neuron number was found in chicks submitted to an unorganized noise. The neuronal  
177 nuclear area increased in the field L but decreased in the auditory nuclei and hippocampus.  
178 Glial cell number significantly increased in chicks submitted to music or noise, with the  
179 highest value in the noise group. So, the effects of sounds are related to its characteristics  
180 (music or noise) [41].  
181

182 Always in chicks, the development of forebrain areas involved in juvenile auditory filial-  
183 imprinting was studied in animals auditory-stimulated by sitar music 10 pf days till hatching.  
184 In the stimulated groups, nuclear areas significantly increased compared to controls, with  
185 difference between music stimulated animals compared to animals submitted to species-  
186 specific sounds. In animals submitted to species-specific sounds, cells immunostained with  
187 anti-parvalbumin (PV) and anti-calbindin D28K (CaBP), a calcium-binding protein, increased  
188 compared to music-stimulated animals. This increase of neurons is certainly linked to  
189 auditory imprinting and learning in chick [42].

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Music would also improve the success of in vitro fertilization [43].

### **3.2.3. Effects of sound and music on the immune system**

The effects of music therapy were investigated in patients with stroke, Alzheimer's disease or Parkinson's disease [44]. At the end of the treatment, the percentage and activity of the Natural Killer cells (NK) of the immune system increased independently of the pathological state. Similarly, rhythmic percussion was causing an increase in natural NK and activating the ratio of dehydroepiandrosterone (DHA) / cortisol, acting on aging. There is no action detected on other parameters. These effects are different from the effects of a simple noise [45]. In individuals submitted to a stressful activity, music increased the feeling of wellbeing. So, a very lively music caused the increase of norepinephrine level, vitality and decreased the characteristics of depression. Active NK cells decreased after 20 minutes of silence. The results of the study showed that different kinds of music and sounds had different effects on immune, neuroendocrine, and psychological responses [46]. In another study, the effects of a recreational music-making were evaluated on male corporate employees. By comparison with controls, the group of persons listening music showed enhanced mood, lower gene expression levels of the stress-induced cytokine interleukin-10, and higher NK cell activity when compared to the control [47].

The effects of gong sound on immune function were studied in rats with Chinese diet-induced Liver (Gan) -Si Stagnation and Spleen-qi Seficiency syndrome (LSSD). The animals were divided into five groups: 1) normal; 2) "LSSD group": rats with induced LSSD rats; 3) "Xiaoyao Powder group": rats with LSSD having received a traditional Chinese mixture of medicinal plants, the Xiaoyao Powder; 4) " Gong-tone group": rats with LSSD subjected to gong sound and 5) "Combined group": rats with LSSD both subjected to gong sound and receiving "Xiaoyao powder". Serum gastrin, phagocytosis by macrophage IgG levels and T cell proliferation decreased in the LSSD group compared to the normal group. The same parameters increased in the "Gong-tone", "Xiaoyao Powder" and "combined" groups, the parameters of the combined group being higher than those of the other two groups [48]. In young rats and adults who became asthmatic after provoking stress, the number of white blood cells and IL-4 increased. Corticosteronemia increased in the stressed adult group, while corticosterone IL-1 $\beta$  increased in stressed youth and then decreased in adults. In young and adult animals, the stress response of the hypothalamic-pituitary-adrenal (HPA) axis was also different. Corticosteronemia and IL-4 were reduced in rats that heard music (Mozart's Sonata K.448) [49]. The effects of music on the immune system were also studied in mouse. The animals were subjected to either noise (wide band of sound) from midnight and / or to music for 5 hours the following morning. Cellularity of the thymus and spleen (cell density), T cell population, splenocyte proliferative response to mitogens (conavalin A), and K cell activity were improved in BALB / c mice subjected to music [50].

The music thus has effects on the immune, endocrine and psychological responses. The music modulates particularly the activity of the NK cells, the cytokines. There are also subtle variations depending on the type of music (lively, slow, percussion, etc.).

A few papers enlightened by Liao [51] described the effects of music on the allograft survival. The effects of music on allograft survival and the establishment of regulatory CD4<sup>+</sup> cells were also studied in an experimental mouse murine transplant model [52,53] Mice rendered deaf (CBA / N strain) underwent transplantation of a heart from another strain (C57BL / 6). The mice were exposed for 7 days to three types of music: an opera (*La Traviata*, Verdi), a classical instrumental music (Mozart) and New Age music. A control group was exposed to one of six different sound frequencies. Allograft survival was

\* E-mail address: [jmexbrayat@univ-catholyon.fr](mailto:jmexbrayat@univ-catholyon.fr); [jean-marie.exbrayat@ephe.psl.eu](mailto:jean-marie.exbrayat@ephe.psl.eu)

243 significantly prolonged in animals exposed to opera and classical music; the survival of  
244 grafts of animals exposed to unique sound frequencies and New Age music was more  
245 limited. Modulations were observed depending on the type of music. Cellular proliferation, IL-  
246 2 and IF- $\gamma$  were suppressed in operably exposed mice, while IL-4 and IL-10 were  
247 upregulated and the cell population CD4<sup>+</sup>, CD25<sup>+</sup>, Foxp3<sup>+</sup> regulators increased. Exposure to  
248 certain types of music can induce a prolonged survival of cardiac allografts and generate  
249 regulatory cells.

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## 251 **4. EFFECTS ON CELL-CULTURES OR ISOLATED CELLS**

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### 253 **4.1. Effects on red blood cells**

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255 Classical music increases the deformability of red blood cells. A fine study has shown that  
256 classical music and rock reduced the aggregation of red blood cells, a little more important in  
257 the case of classical music [54]. This result shows that sound and more especially music  
258 exert effects on the surface properties of these cells. Inversely, the exposure to an  
259 unpleasant, unorganized noise has no particular effect. In human blood cells the activity of  
260 adenylate kinase, a membrane protein essential for the integration of external signals in  
261 cells, increases after exposure to a low frequency field (ELF) and decreases slightly after  
262 exposure to a TAMMEF field (music-modulated [55]). The low frequencies can thus have an  
263 influence on the cellular electrical charge and the stimulation of the adenylate kinase activity  
264 brings the cell to a state of equilibrium. The music acts by maintaining and regulating the  
265 cellular electric charge [55].

266

### 267 **4.2. Osteoarthritis cartilaginous cells**

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269 Human osteoarthritic chondrocytes grown *in vitro* under two- and three-dimensional  
270 conditions were exposed to electromagnetic fields at low frequencies (ELF; 100 Hz,  
271 electromagnetic waves) or music-modulated electromagnetic fields (TAMMEF) [56,57]. The  
272 exposure of cells to both types of vibration improved cell proliferation, did not generate  
273 reactive oxygen species (ROS), did not cause the depletion of glutathione, did not modify the  
274 mitochondrial transmembrane potential and did not induce apoptosis. In addition, the cells  
275 exposed to TAMMEFs presented a better viability compared to the cells exposed to ELFs,  
276 with grouping and improvement of the density of healthy cells in cultures. Differences in  
277 protein expression showed improved stress response, cytoskeletal regulation, and  
278 inflammation. The electromagnetic waves modified with music (TAMMEF) could interfere  
279 positively with the chondrocytes: not only they did not damage them, but they stimulated  
280 their viability by modulating the expression of proteins, the production of ROS (reactive  
281 derivatives of the oxygen) and the apoptosis. The music could help to identify biomarkers  
282 and could allow a new approach to the treatment of osteoarthritis. But let's stay cautious.

283 In other experiments, *in vitro* osteoarthritic chondrocytes were cultivated in standard  
284 conditions or stimulated with IL-1 $\beta$  or IGF1 in order to become between chondro-formation  
285 and chondro-resorption in case of osteoarthritis. In cultures submitted to ELF or TAMMEFs,  
286 the proliferation of cells was enhanced, apoptosis was not induced, ROS were not  
287 generated, there were no changes in mitochondrial transmembrane potential, no glutathione  
288 depletion was observed [58].

289

### 290 **4.3 Tumor cell strain**

291

292 Other work has suggested that music can alter *in vitro* the size and granularity of MCF7  
293 cells, a tumor cell strain derived from breast cancer, by interfering with the binding of  
294 hormones to their receptors, which modulate the physiological processes [27,28]. Music

295 limits the development of pulmonary metastases caused by the injection of these tumor cells  
296 [50].

297

## 298 **5. THE HARMFUL EFFECTS OF NOISE**

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300 The effects of music could be special cases of sound effects on cells. Works show that any  
301 type of sound can have or not beneficial effects. There are sounds with harmful effects, this  
302 is the case of noise, a set of unpleasant sounds in the ear and, as we will see, causes  
303 disturbances at the most unexpected cellular level. A review summarized the effects of  
304 different levels of noise resulting from certain leisure activities: exposure to very strong  
305 music, being rock, classical or jazz; exposures from personal listening devices; noise around  
306 houses, gunshots or target shooting. The greatest threat to hearing comes from these last  
307 sounds [59].

308

309 The effects of sound pulses were studied on epithelial cells of the choroidal plexus of rats.  
310 The animals were exposed to impulses every 20 minutes 10 times a day for one month. At  
311 the end of the experiment, the choroidal plexuses were removed and examined by histology.  
312 Compared to controls, the number of normal cells decreased and the number of apoptotic  
313 cells increased. The noisy impulses thus caused the apoptotic death of the choroidal plexus  
314 cells [60]. In another experiment, rats were exposed to rock music at 80 decibels for 24  
315 hours, during which control animals were kept in their usual environment [61]. Leukocyte  
316 subpopulations were obtained and stimulated *in vitro*. Neutrophils and macrophages in  
317 noise-exposed animals secreted significantly less superoxide and interleukin-1 than control  
318 animals. The short-term exposure of rats to noise modified some of the functions of  
319 leukocytes [61].

320

## 321 **6. DISCUSSION AND CONCLUSION**

322

323 Research on the effects of music on cells is an expanding field. It has long been known that  
324 music has beneficial effects to calm stress, anxiety, and even pain. Studies on the effects of  
325 sound vibrations on auditory cells have been conducted for a long time [62]. More recently,  
326 more and more works about the effects of music on non-auditory cells have been published.  
327 Thus, the effects on growth, apoptosis, action of proteins, immune system in animal, plant  
328 and bacterial cells could be demonstrated. These effects, which contribute to favoring  
329 positive emotions, are of a physiological nature and require molecules and physicochemical  
330 mechanisms. The molecules involved include neurotransmitters, hormones, cytokines and  
331 peptides.

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333 The music affects the immune, endocrine and psychological responses. The music  
334 modulates in particular the activity of the NK cells and the cytokines. There are also subtle  
335 variations depending on the type of music (lively, slow, percussion, etc.). The effects of  
336 sound and more particularly music have been used for therapeutic purposes. The Mozart  
337 effect can be resumed based on these works. According to the 1993 publication of Rauscher  
338 et al. [63] the Mozart effect concerns the improvement of reasoning skills in normal subjects  
339 after listening to Mozart's K 448 piano sonata. In 2014, Pauwels et al. have taken up this  
340 effect by considering that music can modulate the immune response by increasing the  
341 activity of NK cells, lymphocytes and interferon- $\gamma$  [64]. Appreciated music would help to  
342 strengthen the immune system and to change stress, reducing it. Finally, the effect of music  
343 used to reduce stress, heart rate, blood pressure and to distract the patient could be related  
344 to the effects on the immune system [64].

345

346 Experiments have been performed in order to discover the effects of music on several  
347 aspects of biology and physiology, and several papers have been published about very

348 different subjects. For example, in rat, 432 Hz and 440 Hz musical frequencies increased the  
349 expression of Ghrelin (Ghre), a peptide secreted from the stomach under fasting conditions,  
350 inducing food intake. This peptide stimulating appetite through neuropeptide Y, it seems that  
351 musical frequencies could affect food intake by modulating the hypothalamic Ghre  
352 expression and release [65]. In urethane-anesthetized rats, renal sympathetic nerve activity  
353 (RSNA) on blood pressure decreased in subjects listening *Traumerei* by Schumann. In  
354 anesthetized rats, such a musical stimulation caused an elevation of gastric vagal nerve  
355 activity and increased the c-Fos labeled cells of the auditory cortex [66,67].  
356

357 A compilation of published studies concerning numerous vertebrate species permitted to  
358 identify several candidate genes allowing one to give a molecular basis of musical traits [68].  
359 Besides these studies, the importance of the effects of music has been understood since a  
360 long time. Several publications concern the effects of music therapy. Without being  
361 exhaustive, several recent works are related to the increasing of altruism through the  
362 regulation of steroid hormones by music [69]. Use of music gave positive results in the  
363 treatment of patients undergoing allogeneic hematopoietic stem cell transplantation,  
364 providing welfare of patients [70]; some experiments have been performed in animal in order  
365 to understand the mechanisms implicated [71].  
366

367 Finally, a lot of current studies concern the effects of sound and more especially music upon  
368 the organisms. These studies belong to different domains of research. Some of them - the  
369 most numerous – are devoted to the effects on the brain through the auditory cells. Others  
370 concern the effects directly upon the non-auditory cells. Certain works were performed on  
371 vegetal or animal organisms, others directly on cells themselves, using cell cultures. Few  
372 works concern eukaryotic unicellular organisms. Results of these studies show music and  
373 sound exert true effects on the physiology. But the experiments and results are still well  
374 disparate, with effects on organisms via auditory cells, on non-auditory cells, sometimes  
375 involving both auditory and no auditory cells, and with the use of different music according to  
376 the culture of the country where the study has been done.  
377

378 In conclusion, nevertheless this large variation of works or results, the study of the effects of  
379 sound and especially music on the cells is a subject on the future, considering the immense  
380 possibilities offered by music in modulating the physiology, with potential therapeutic  
381 application.  
382

## 383 **ACKNOWLEDGEMENTS**

384  
385 The authors thank Lyon Catholic University which supported this work.  
386

## 387 **COMPETING INTERESTS**

388  
389 Authors declared that no competing interests exist.  
390

## 391 **AUTHORS' CONTRIBUTIONS**

392  
393 Claire Brun and Jean-Marie Exbrayat participated in an equal work in realizing the review.  
394 JME wrote the draft of article, CB corrected it, CB and JME wrote the definitive manuscript.  
395

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