

Technological prospecting of music therapy in Alzheimer's disease

Prospecção tecnológica da musicoterapia na doença de Alzheimer

Prospección tecnológica de la musicoterapia en la enfermedad de Alzheimer

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Abstract

Alzheimer's disease (AD) is characterized by cognitive impairment and progressive memory loss and drug treatments have limited efficacy. Thus, non-pharmacological interventions, such as music therapy, have shown to be promising as supporting pharmacological treatment and, therefore, may arouse commercial interest regarding the development of this type of product. Thus, this study aims to carry out a patentometric survey on patent registrations with music therapy in the treatment of AD. A systematic search was carried out from 2000 to 2020 on the Orbti-Questel website, searching for documents referring to music therapies in AD. The terms “Alzheimer music methodology active therapy” and “Alzheimer music methodology passive therapy” were used. After searching, reading, and excluding duplicate results, we found four patent families referring to music therapy in AD and all were selected as a result, which was considered little compared to the number of studies published on the subject.

Keywords: Alzheimer; Music; Therapy.

Resumo

A doença de Alzheimer (DA) se caracteriza por comprometimento cognitivo e perda progressiva de memória, sendo os tratamentos com fármacos de eficácia limitada. Neste sentido, intervenções não farmacológicas, como a musicoterapia, têm-se mostrado promissoras como coadjuvantes ao tratamento farmacológico e por conseguinte, podem despertar o interesse comercial no que concerne ao desenvolvimento deste tipo de produto. Assim, este trabalho objetiva realizar um levantamento patentométrico sobre registros de patentes com musicoterapia no tratamento de DA. Foi realizado uma busca sistemática nos períodos anuais de 2000 a 2020 no site Orbti-Questel, e para a busca de documentos referente a terapias musicais na DA utilizou-se os termos: “Alzheimer music methodology active therapy” e “Alzheimer music methodology passive therapy”. Após a busca, leitura e exclusão de

resultados duplicados, foram selecionadas como resultado quatro famílias de patentes referindo-se à terapia musical na DA, o que foi considerado pouco frente a quantidade de estudos publicados sobre o tema.

Palavras-chave: Alzheimer; Música; Terapia.

Resumen

La enfermedad de Alzheimer (EA) se caracteriza por deterioro cognitivo y pérdida progresiva de la memoria, y los tratamientos farmacológicos tienen una eficacia limitada. En este sentido, las intervenciones no farmacológicas, como la musicoterapia, han demostrado ser prometedoras como soporte del tratamiento farmacológico y, por tanto, pueden despertar el interés comercial en cuanto al desarrollo de este tipo de productos. Así, este trabajo tiene como objetivo la realización de una encuesta patentométrica sobre registros de patentes con musicoterapia en el tratamiento de la EA. Se realizó una búsqueda sistemática de 2000 a 2020 en la web de Orbti-Questel, y para la búsqueda de documentos referentes a musicoterapias en la EA se utilizaron los términos: “Metodología musical Alzheimer terapia activa” y “Metodología musical Alzheimer terapia pasiva”. Tras buscar, leer y excluir resultados duplicados, se seleccionaron como resultado cuatro familias de patentes referentes a la musicoterapia en la EA, lo que se consideró poco comparado con la cantidad de estudios publicados sobre el tema.

Palabras clave: Alzheimer; Canción; Terapia.

1. Introduction

The increase observed in the elderly population worldwide is also accompanied by a rise in the number of elderly people diagnosed with dementia. Approximately 50 million people have been given this diagnosis (Alzheimer's disease international, 2019). Alzheimer's Disease (AD) is the most common dementia (Nichols et al., 2019), which can be defined as a complex and insidious neurodegenerative disease, in which the first symptoms appear even before the probable diagnosis. The main characteristic is intense synaptic degeneration and neuronal loss, leading to a progressive and constant decline in communication, memory and orientation functions (Atri, 2019 and Tiwari et al., 2019).

Since the evolution of AD symptoms causes a progressive and irreversible loss in the autonomy of patients and that the main function of the drug treatment of the disease only attenuates and mitigates the progression of symptoms of this pathology (Olazarán et al., 2010), the search for alternative and non-pharmacological therapies, at a lower cost, can contribute to increasing the quality of life of patients with AD.

Music therapy is a type of non-pharmacological intervention that applies the effects of sounds, music, and movements, which theoretically integrate with cognition and behavior, stimulating interpersonal relationships, non-verbal communication, creativity, emotions, and psychiatric symptoms (Cooke et al., 2010; Lyu et al., 2018 and Raglio et al., 2010). When listening to familiar songs, elderly people's memory is activated, thus stimulating areas inside and outside the temporal lobe, including frontal and parietal regions (Jacobsen et al., 2015; and Platel et al., 2003 and Satoh et al., 2006).

Therefore, as there are possibilities for adjuvant therapies, such as music therapy, which has a lower cost compared to pharmacological treatment, in addition to being more accessible, it is also necessary to investigate whether new methods based on music therapy are being patented to predict and, perhaps, prevent an increase in the cost of this type of treatment. Therefore, this article aims to review the patents filed on using music therapy as a treatment for Alzheimer's disease.

2. Methodology

The methodology used in this article is quantitative and qualitative, as it sought to quantify the patents that would be in the scope of the study at first, and then the patent documents were read to ascertain which would be suitable for the study.

The methods used to search for patents were the "state-of-the-art search", which is essentially a survey of all relevant documents published in a particular field or fields or patents filed in a particular field or fields, or patents filed by particular applicants or inventions invented by particular inventors (Clarke, 2018).

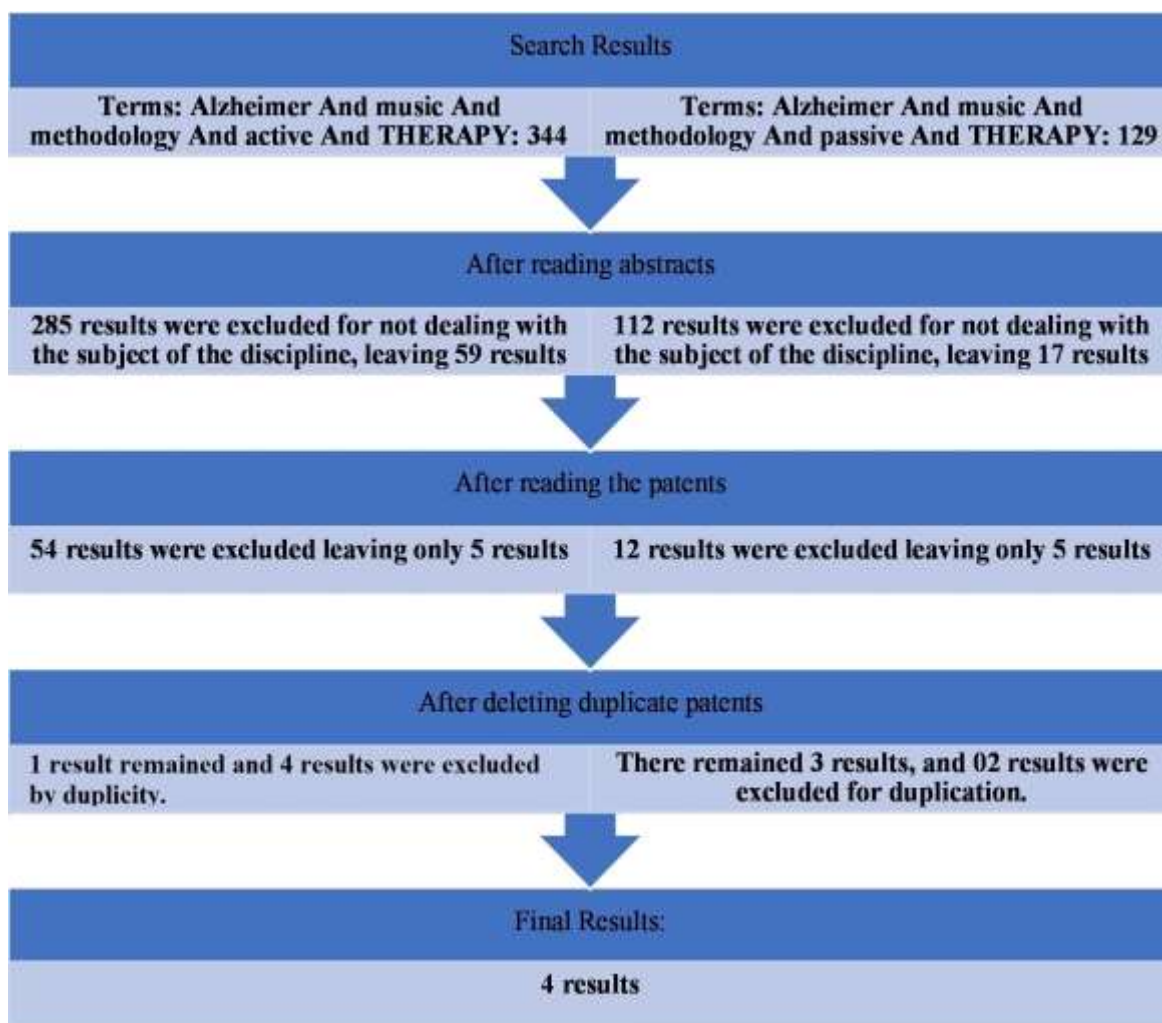
The prospective analysis was performed based on patent filings from 2000 to 2020, in the Orbti-Questel database, which is considered a quantitative and qualitative study, because in addition to the number of registered patents, a qualitative

analysis of the inventions was carried out based on studies published so far with the methodology or proposal of each invention.

It is important to note that the 2020 data are partly due to the patent analysis period. For the survey of patent documents related to the application of music therapy for the treatment of Alzheimer's Disease, the search fields "Easy Search" and the keywords below were used, together with truncation symbols such as quotation marks and Boolean operators, to help us find as many documents as possible: "Alzheimer music methodology active therapy" and "alzheimer music methodology passive therapy".

The patent selection method for this work was as follows:

Figure 1- Patent search methodology



Source: Authors (2021).

Based on search, the patents are listed below:

Table 1 - Search results.

FINAL SEARCH RESULTS		
Order Number	Publication Number	Title
01	EP2729931	Method and system for analysing sound
02	US9480812	Methodology, system, use, and benefits of neuroacoustic frequencies for assessing and improving the health and well-being of living organisms
03	US20100191037	Iso music therapy program and methods to use it
04	US20070137463	Digital music composition device, composition software and method of use

Source: Authors (2021).

The survey was carried out in June, July, and August 2020.

3. Results

Technological prospecting was used as a tool to systematically map scientific and technological development, which are capable of significantly influencing an industry, the economy, or society as a whole (Serafini et al., 2012).

The word “Alzheimer” generated 56,964 results in the Questel-Orbit database.

Table 2 - Search for patents deposited in the Questel-Orbit database by keywords.

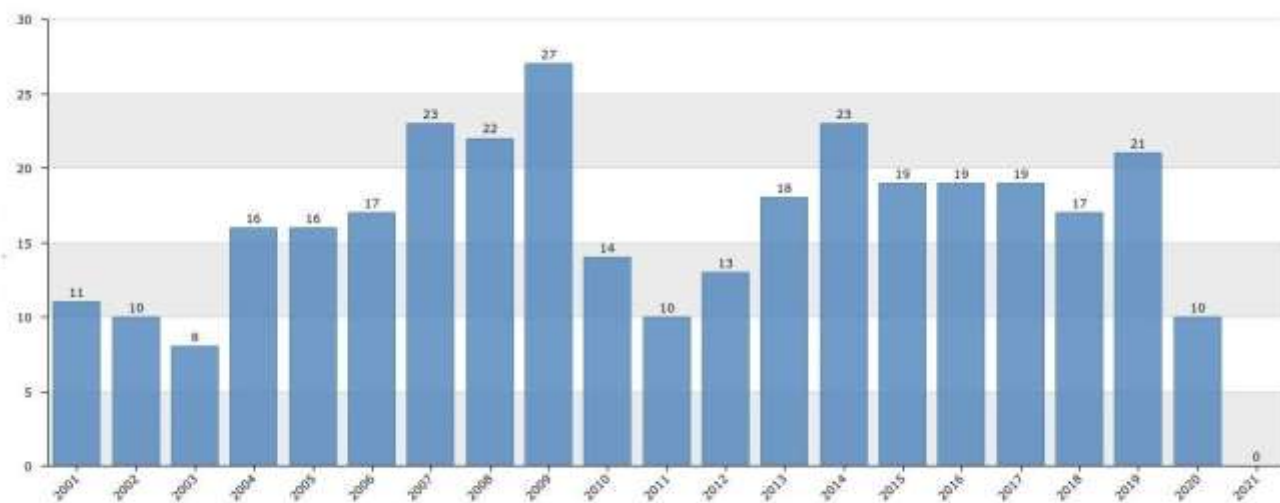
Keywords	Results	Keywords	Results
“Alzheimer”	56.964	“Alzheimer” and “Music” and “Therapy” and “Non-pharmacological”	0
“Alzheimer” and “Disease”	55.130	“Alzheimer” and “Music” and “Therapy”	1368
“Alzheimer” and “Intervention”	1294	“Alzheimer” and “Music” and “Methodology” and “Active” and “Therapy”	344
"Alzheimer" and "treatment"	41810	“Alzheimer” and “Music” and “Methodology” and “Passive” and “Therapy”	129
“Alzheimer” and “Music” and “Therapy” and “Non-Pharmacological” And “Intervention”	42	“Alzheimer” and “Methodology” and “Music “and “Passive” or “Active” and “Therapy”	346

Source: Authors (2021).

Henceforth, an overview of patents will be traced through graphics extracted from Questel-Orbit using the terms “Alzheimer” and “Methodology” and “Music” and “Passive” or “Active” and “Therapy”:

Figure 2 illustrates the evolution of published applications over time, showing the dynamics of inventiveness of the technology studied for Alzheimer's disease. Between the period studied there is a constant publication of patent families. The bar chart shows a peak in 2007 (n=23), 2009 (n=27), and 2014 (n=323), which shows continued interest of the actors in the field.

Figure 2 - Patent families.
Number of patent families/Application in first year

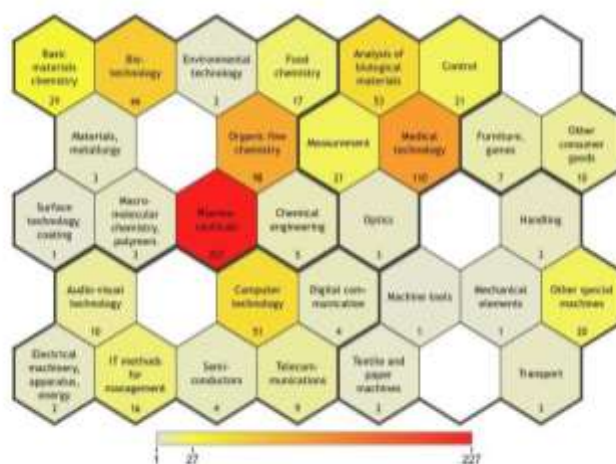


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Source: Questel-Orbit (2021).

Concerning the Technological Domain (Figure 3), the patent deposits in the areas of Pharmaceuticals (227), Medical Technology (110), and Fine Organic Chemistry (98) stand out, showing that most of the patents initially surveyed (more than half) are in the three areas cited, which demonstrates the interest of large applicants in protecting their technologies in such domains.

Figure 3 - Technological Domain.



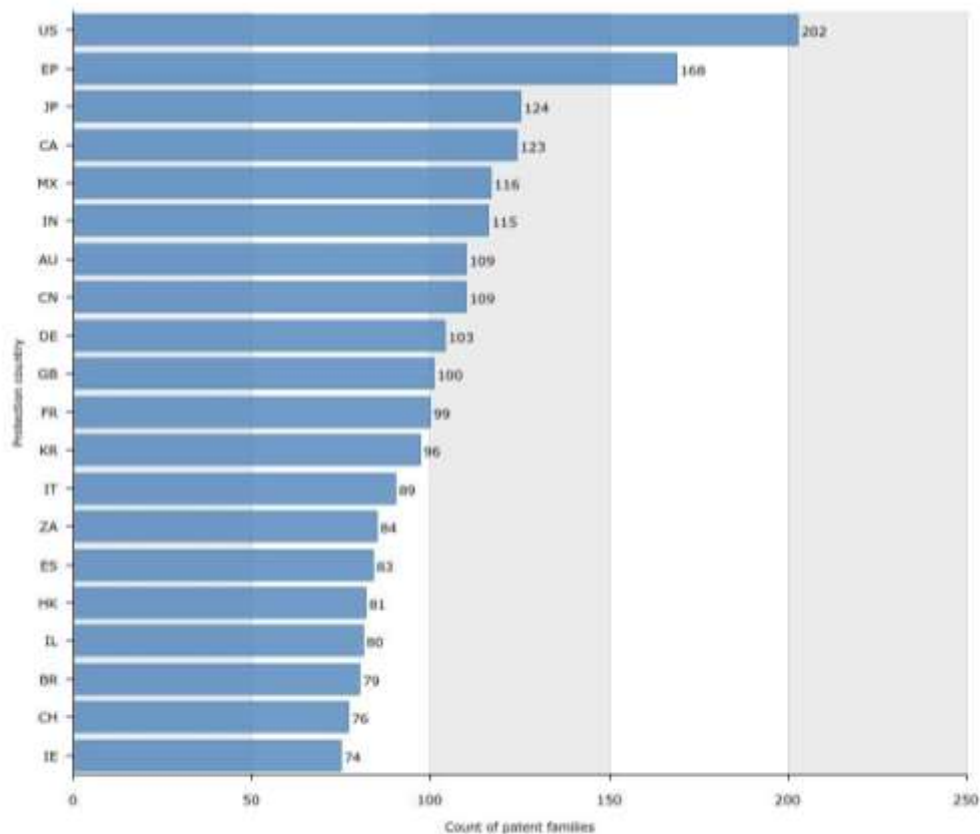
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Source: Questel-Orbit (2021).

In terms of protection by country, we observed the countries that most filed patents such as the USA (202), the European Patent Office (168), Japan (124), Canada (124), Mexico (116), India (115), Australia (109) and China (109) as shown in Figure 4. This information shows which markets are the most attractive for depositors to protect their technologies to maximize profits. It also enables us to know which markets are under explored, which technologies are not protected there, and

to take advantage of the moment to register such patents, not protected, by third parties, as patents follow the territoriality principle.

Figure 4 - Protection by Country.

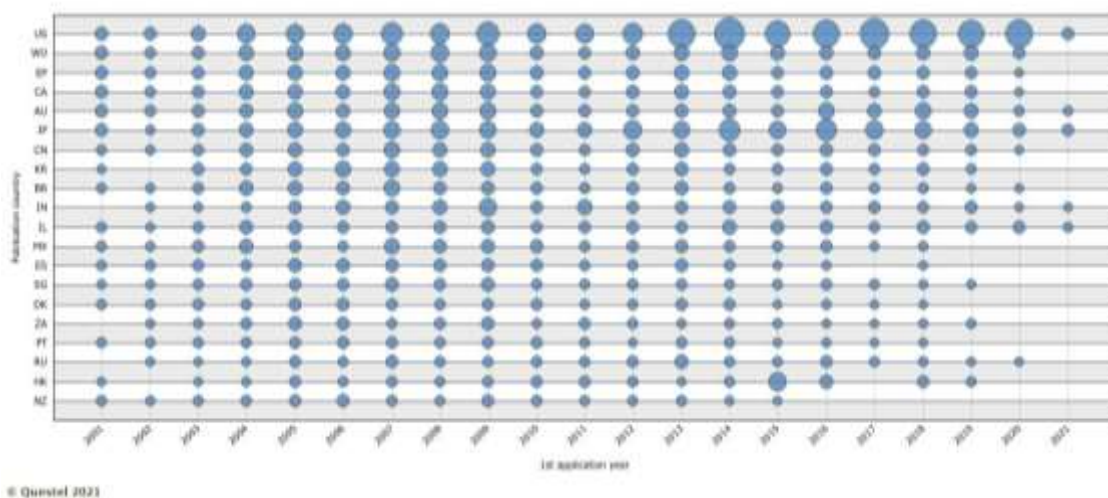


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Source: Questel-Orbit (2021).

In terms of publications per country/year, the average number of patent publications tends to remain stable worldwide. Considering the markets, there was a large number of publications in the US in 2007, 2009, between 2013-2020, in Japan between 2012-2019, and in Hong Kong in 2015, as shown in Figure 5.

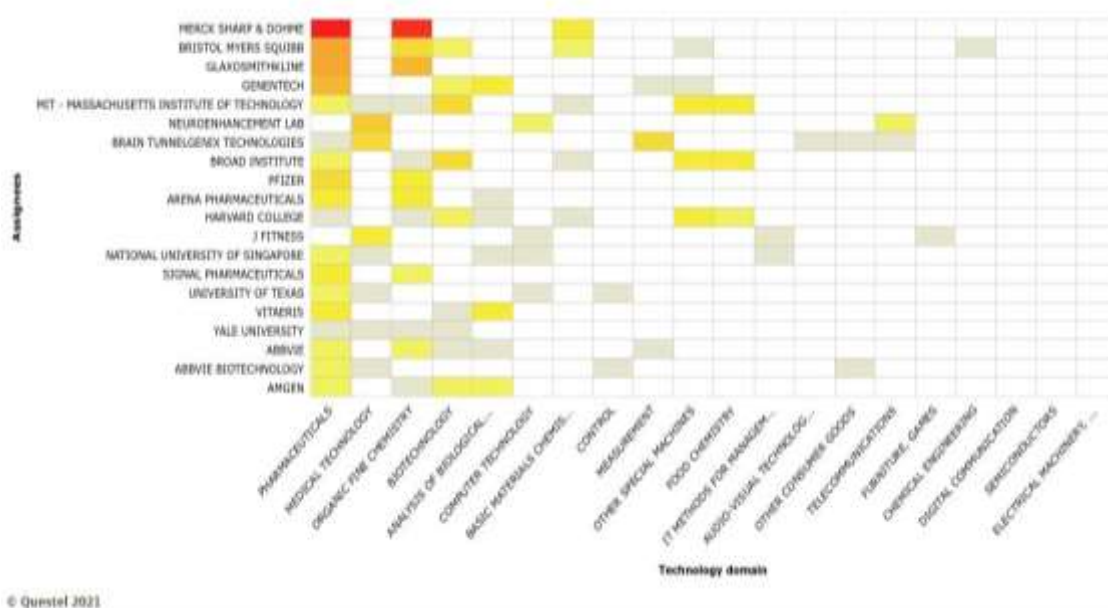
Figure 5 - Publications by Country/Year.



Source: Questel-Orbit (2021).

Concerning Depositors by Technological Domain, almost all depositors made deposits in the area of Pharmaceuticals and Fine Organic Chemistry, and to a lesser extent in Medical Technology, as shown in Figure 6. Only MIT and Yale University have published patents in the three areas mentioned, which are renowned public research centers. In the private sector, Merck Sharp & Dohne, Bristol-Myers Squibb and GlaxoSmithKline stand out in Pharmaceuticals and Fine Organic Chemistry, which are respectively global pharmaceutical, chemical, and life sciences companies found in 67 countries, with headquarters in the USA. Bristol-Myers Squibb (BMS) is an American Pharmaceutical Industry, whose headquarters are in New York City. This company makes prescription medicines in various therapeutic areas, including cancer, HIV/AIDS, cardiovascular disease, diabetes, hepatitis, and rheumatoid arthritis. GlaxoSmithKline is a British multinational pharmaceutical company that produces biotechnology products, healthcare products, and vaccines. The headquarters are in London.

Figure 6 - Depositors by Technological Domain.



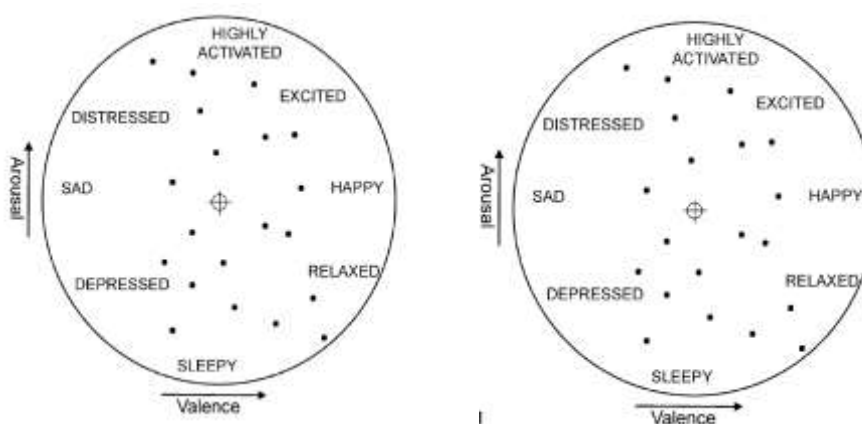
Source: Questel-Orbit (2021).

Henceforth, the patents mentioned in the methodology will be described:

a) EP2729931, filed at the European Patent Office, published on 10 July 2020, CIP Code G06F 16/683, (ELECTRIC DIGITAL DATA PROCESSING using metadata automatically derived from the content). The title is “Sound analysis method and system” and the depositor is X-System Limited, Holmbury. The invention is a method and system for analyzing sound (e.g., music tracks). The invention proposes to predict the psycho-affective responses that music tracks and sounds cause in the listener, plotting data related to affective valence and activation, using harmony, turbulence, rhythmicity, sharpness, and volume as parameters of the analyzed sounds. Affective valence and arousal predictions were validated using heart rate variability (HRV) as physiological parameters, considering empirical evidence that positive valence is associated with high vagal power and with high HRV, and that negative valence is associated with low HRV, indicating a low vagal power. In addition to the analysis, the system also used Galvanic Skin Conductance data to validate the predictions.

The invention is based on passive listening, which categorizes the songs and classifies them, plotting them in a circumplex type graph, where one axis is dedicated to valence (X-axis) and another axis is dedicated to activation (Y-axis). The combination of these results in mood states are shown in Figure 7.

Figure 7 - Valence x Arousal Graph.



Source: Patent EP2729931.

b) US9480812, filed with the US Patent Office, published on November 1, 2016, CIP Code A6 IB5/04 (bioelectric signal measurement from the body or parts (electrically conductive preparations for use in therapy or testing) in vivo A61K 50/00); A61M 21/02 (DEVICES FOR PRODUCING OR ENDING SLEEP OR STUPOR) and A61M 21/00 (other devices or methods for causing a change in the state of consciousness; Devices for producing or ending sleep by mechanical, optical, or acoustical means, for example, for hypnosis). Its title is “d” and the applicant is Jeffrey D. Thompson. This invention concerns the treatment of patients using sonic, optical, or vibrational energy applications to affect patients' mental, emotional or physiological state, using manual, semi-automated, or fully automated systems, or any combination thereof, to favor emotional and physical conditions.

The invention specifically aims to act on the autonomic nervous system (ANS), seeking stimuli that cause a balance between the sympathetic (SNS) and parasympathetic (PNS) nervous systems, which are monitored through continuous assessment of heart rate variability (HRV). Using headphones, that is, it is a passive methodology, the invention applies sound frequencies to the listener and in parallel, the light system also provides stimuli. According to the description of the invention, the body would tend to try to match the received frequencies, thus regulating the heart and respiratory rate and brain waves. Regarding brain waves, the invention states that when applying frequencies with differences, even if small (around 5Hz)

between one ear and another, it induces the brain to tune the two hemispheres. Therefore, using sound and light stimuli in parallel with ANS monitoring, the device assesses the moment when the individual reaches homeostasis between the SNS and the PNS, which would bring benefits to the listener.

c) US20100191037, filed with the US Patent Office, published on July 29, 2010, Codes CIP Int. Cl. A61M 21/00. (DEVICES FOR PRODUCING OR ENDING SLEEP OR STUPOR), G09B 19/00 (PROCESSING ELECTRICAL DIGITAL DATA) and G06F 3/048 (ELECTRICAL DIGITAL DATA PROCESSING). The title is “ISO music therapy program and methods for using the same” and the depositor is the University of Texas System. This invention refers to using music in cancer therapy and other conditions and is a computer-implemented method to modulate a mood state in a person, including selecting an appropriate target mood, filtering a list of tracks, music based on an initial mood, and vectoring through additional filtering of the tracklist to assign the music tracks, creating a progressive mood modulation from the initial mood to the target mood. The invention aims to induce states of relaxation and stress reduction, which was designed for cancer patients, but which can be applied to any individual. In general, the invention uses a classification of a certain number of songs according to rhythm (BPMs) and orders them in a list to be played to achieve a previously chosen goal. One of the examples given is that of reduction in a stressful situation, where the system chooses songs (among those available) that gradually reduce their BPMs so that the individual can reduce acute stress. It is also a passive listening method.

a) US20070137463, filed with the US Patent Office, published on June 21, 2007, with CIP Int Codes G10H 7/00 (ELECTROPHONIC MUSICAL INSTRUMENTS; INSTRUMENTS IN WHICH THE TONES ARE GENERATED BY ELECTROMECHANICAL MEANS OR ELECTRONIC GENERATORS, OR IN WHICH THE TONES ARE SYNTHESIZED FROM A DATA STORE). The title is “Digital Music Composition Device, Software and Composition Method of Use” and the depositor is David Lumsden. The invention concerns an electronic device that is particularly useful in the fields of Music Therapy. The invention is a computer system or program, which can also be in an app format, where the individual makes musical compositions by superimposing sound patterns (instruments, rhythms, etc.) previously saved in the device, thus characterizing an active method. In addition, the system would provide a kind of social network for sharing compositions, thus promoting a greater relationship between users. The benefits of the invention, according to the description of the invention, are the same as those of music therapy, such as promoting well-being, managing stress, relieving pain, expressing feelings, improving memory and communication.??

4. Discussion

There is still no drug treatment that can stop the progression of the disease. Thus, non-pharmacological interventions can be an alternative for cognitive rehabilitation, especially those that promote the individual's brain stimulation. Music therapy can be found in active aging programs offered to the elderly population. The scientific recognition, deposited in the idea of this methodology, is given as the literature shows results that benefit the patient in reducing the symptoms of AD individuals, showing results at the physical, cognitive, and psychological levels (Gallego and García, 2017).

Despite the need for alternative and non-pharmacological therapies to act as an adjunct in the treatment of AD, globally, this patent search found only 4 registered patents related to the use of music therapy for this purpose. This result contrasts with the benefits described in the literature related to this type of intervention, which, based on the moderate effects shown by anticholinesterase drugs and memantine on cognitive function and, in high doses only, varied effective and no effect on neuropsychiatric symptoms (Gómez and García, 2017 and TAN et al., 2014). It is a promising non-pharmacological alternative treatment, showing improvement in the cognitive function and behavior of AD patients (Olazarán et al., 2010 and Seitz et al., 2012).

Music therapies promote cognitive and motor effects that are related to music processing through auditory functions,

motor coordination, cognitive and emotional processes. They act concentrically in the right and left cerebral hemispheres, with distinct hierarchies developing cerebral plasticity. Auditory memories are stored in the temporal lobe; however, this area is affected by the disease, thus the experience of listening was studied based on the idea that listening and remembering are mechanisms that act in different parts of the brain. Brain mapping was performed using biomarkers such as cortical atrophy, hypometabolism, and amyloid-beta plaque accumulation. The results suggest the preservation of musical memory and describe that the region has a lower rate of hypometabolism and cortex atrophy. Moreover, they have concentrations of beta-amyloid, however, the area is preserved and working with some efficiency (Jacobsen et al., 2015).

Regarding the inventions described in this article, we sought articles in the literature review that could support them. Although the description of the invention already contains a theoretical basis, we believe it is important to carry out this procedure.

Inventions whose main objective is to reduce agitation, stress or that aim at greater relaxation, namely, EP2729931, US9480812 and US20100191037, are supported by studies such as the one by Ridder et al. (2013), using a sample of 42 individuals, randomly, for 6 weeks, and that received standard treatment with psychotherapeutic drugs and music therapy. The variables analyzed were agitation, quality of life and medication. Agitation increased in standard treatment (medication) and decreased during treatment with music therapy. The prescription of use of psychotropic drugs increased during standard treatment than with music therapy treatment, demonstrating that six weeks of treatment has a reduction in agitation, however, the positive results concerning the frequency of agitation and quality of life need to be evaluated with larger samples. Furthermore, Ortí et al. (2018) applied a music therapy protocol to treat individuals with mild AD to stimulate the socio-emotional area and found results that suggest a significant improvement in depressive symptoms and stress, which improve with levels of decrease in the amounts of cortisol, one of the major stress-related hormones, which indicates that once this component decreases, there is also a linear decline in stress and depression levels. Another study by Lyu et al. (2018) evaluated the effect of music therapy in patients with mild, moderate, and severe AD over 3 months with interventions based on active listening, singing along with songs, reading lyrics, and a control group, without any intervention. All songs and lyrics were previously chosen by the elderly through a musical preference survey. The group of elderly people who listened to and sang the songs showed, after 3 months, improvement in verbal fluency, psychiatric symptoms, and memory, but did not show improvement in activities of daily living.

Regarding methods to assess the mood state during music therapy sessions that use monitoring the sympathetic and parasympathetic autonomic nerve system as a method (e.g. inventions EP2729931 and US9480812), which is a measure of states of relaxation and agitation, the inventions can be corroborated by the study carried out by Iwanaga, Kobayashi and Kawasaki et al. (2005), who evaluated the effect of low- and high-frequency music and calming/sedative music and excitatory music, compared to music conditions in young people. The study found that different frequency patterns and music provoke different heart rate variability responses and that this is associated with activities of the sympathetic and parasympathetic systems, indicating situations of stress or relaxation.

The intervention proposal of one of the selected inventions, US20070137463, is musical composition, which can be considered as an active strategy. Interesting results can be found in the literature regarding active interventions, such as the study by Giovagnoli et al. (2018), who evaluated the effect of treatment with an anticholinesterase inhibitor (memantine) alone or associated with active music therapy, where the elderly actively participated in the sessions, playing instruments, for example. The music therapy group showed significantly better improvement compared to the memantine-only group of appetite and depression scores. In addition, significantly fewer patients in the music therapy group had worsening depression scores (Neuropsychiatric Inventory-Questionnaire - NPI). However, this study did not find superiority of music therapy plus memantine compared to memantine alone, in relation to the language factor. Another case-control study by Svansdottir and

Snaedal (2006) investigated the effects of active music therapy as a non-pharmacological treatment in patients with moderate and severe AD.

Patients listened to the music through a good quality speaker, in 2 weekly sessions of 45 minutes each. The sessions included various activities: “welcome music” (patients had to greet and introduce themselves), rhythmic accompaniment activities with clapping and musical instruments (triangles, tambourines, and maracas), movements with background music, recognition games, music and interpreters (musical bingo) and the farewell song. Patients showed improvement in anxiety and agitation disorders, but not in other criteria assessed by the study questionnaire (BEHAVE-AD). However, it should be noted that the proposal of the invention US20070137463 is quite different from the interventions in the literature, especially because it is a kind of application or computer program for the composition of music, which makes further conclusions difficult.

In a literature review, Leggieri et al. (2019) pointed to the neural mechanisms of music therapy for the treatment of mental health, suggesting that there are aspects of music therapy that lead to positive neurobiological changes and improvements in mental health. These aspects are participant comfort at the start of the treatment, using emotionally positive music, improved confidence in the participant-therapist relationship, access to participant emotions through referential music therapy, memory recall through autobiographically relevant music, change in unwanted behavior patterns, and improvement of the social aspect.

However, this area of knowledge still needs more studies that assess in more detail both the mechanisms involved in the treatment of music therapy in AD and the supposed benefits of this treatment strategy, especially better-controlled studies with more standardized methods of intervention, and with longer durations; if possible greater than 24 weeks.

5. Conclusion

This study proposed to review patents registered so far in the use of music therapy as a supporting treatment for AD and to carry out an analysis of the theoretical basis of these inventions. After applying the inclusion and exclusion criteria, we found only 4 inventions registered for this purpose, including some older ones regarding the technology used, which can bring different interpretations and conclusions, ranging from little chance of success in the market to a greater need for better-controlled studies and, above all, with standardized interventions.

It is estimated that the number of people affected by dementia doubles every 20 years. Among these dementias is AD because population aging is a reality in most developed countries and even in some underdeveloped ones. It is expected that research on new interventions and technologies will continue to occur as a form of treatment, thus enabling a study that allows for the monitoring of innovations in the area of music therapy in the treatment of AD, production of specialized literature on the subject, with more standardized methods of intervention, and with durations longer than 24 weeks.

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