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Antidepressants Versus Music Therapy: Which Treatment Is Better for Treating Depression in Parkinson's disease?

Emaan Dawood
The Honors College
Virginia Commonwealth University
907 Floyd Ave
Richmond, VA 23284 USA

Faculty Advisor: Faye Prichard

Abstract

Music and medicine are beginning to merge as possible treatment for depression in Parkinson's disease (PD) patients. Antidepressant medication treatment, the standard form of depression treatment for PD patients, demonstrates ambiguous effects in clinical trials, thus warranting a search for other treatments like music therapy. Therefore, a literature review was conducted to understand how music or antidepressant medication therapy affects depression in the PD population. To evaluate antidepressant or music therapy treatment on depression and mood in PD patients, sources via PubMed were obtained and a set of inclusionary criteria, specified in the paper, were utilized for inclusion in this literature review. More inclusionary criteria were considered (e.g. that depression was diagnosed in accordance with NIH recommendations, that severity of depression was established, etc.). However, the consideration of more criteria would have significantly limited the articles to be included in this paper. The results from the search were then compared both qualitatively (if qualitative information was provided) and quantitatively by calculating the Cohen's *d* effect size between the pre- and post- patient-reported outcome measures to determine the magnitude of the experimenter effect. A total of six articles were identified to be included in this literature review. This literature review indicates mixed results on depression and mood for both music therapy and antidepressant treatment as indicated by variability in effect size. Given mixed results, paucity of studies, and small sample sizes, more research will be needed before conclusions can be garnered. To promote the systematic study of the treatment of depression within this population, future researchers should utilize sensitive patient-reported outcome measures to evaluate improvement in mood, utilize formal methods for diagnosis of depression and severity in PD patients, and obtain larger sample sizes for improved statistical power.

Keywords: Parkinson's Disease, Depression, Music Therapy

1. Introduction

Parkinson's disease (PD) affects thousands of people nationally and even more worldwide, being the second most common neurodegenerative disease with motor and nonmotor symptoms.[1] Motor symptoms can include abnormal gait and dysphagia, while nonmotor symptoms can include sleep disorders and depression. About 40-50% of people who experience PD also experience clinically significant depressive disturbances.[2] Regardless of the high percentage of clinical depression occurrence in people with PD, most treatments focus on the motor symptoms of the disease. Nonmotor symptoms, however, can severely influence the treatment of motor symptoms as a patient's mental health can subconsciously impact the way the patient reacts to treatment. Therefore, more emphasis needs to be placed on the nonmotor symptoms of PD and developing effective treatment modalities for people who have PD and depression. With untreated depression, the cognitive and motor symptoms of PD may be more difficult to treat.

Treatment for depression in patients with PD is currently difficult, since there is a lack of studies and research regarding the efficacy of treatments of depression in people with PD. Despite the paucity of studies on this topic,

antidepressants are used as a standard depression treatment for patients with PD. The search for effective treatment methods for depression in people with PD is ongoing and critical to caring for the health of those who have PD. Better treatments for depression in PD can be discovered by comparing and contrasting different treatment types to determine whether one treatment is more efficacious than the other. Without this process, the scientific community may never know the various treatment options that could potentially be effective at treating depression in people with PD. The study of depression specifically in PD is important as its own category because depression works differently in people who have PD compared to people without PD.

Music therapy is one of the treatments that is currently being explored for its effects on various symptoms of PD. Music therapy has been utilized in the field of medicine for various purposes and has recently become more prominent in the context of PD. Music therapy has been explored within the PD field for treating motor and nonmotor symptoms like depression, but there is still a limited number of studies regarding music therapy and depression in people with PD. Medications have long been used as the primary mode of treatment for most medical conditions, but as the field of medicine has grown and evolved, so have treatment modalities. Forms of therapy, like physical or occupational therapy, have become more prominent as adjuvant or primary forms of treatment. As such, music therapy is gaining prominence within the rehabilitative, psychological, and medical fields in general and in the context of PD. Even though antidepressants are the universal clinical treatment of depression, their supposed benefits do not reach their maximum potential in treating depression of people who have PD. Therefore, better PD depression treatments are needed, and music therapy is beginning to show promise in this avenue. Music therapy should, therefore, be further assessed as a potential alternative or adjuvant treatment method for patients with depression and PD.

2. Background

PD is a neurodegenerative disease with an unclear cause. According to the National Institute of Health, the cause of PD involves the death of nerve cells and neurons that produce dopamine, a neurotransmitter in the brain.[3] Therefore, less dopamine in the brain is produced, which results in the motor disturbances associated with PD.[3] The cause of PD is still not exactly clear because scientists currently do not know what exactly causes dopaminergic neurons to die.[3] Since PD is characterized by a lack of dopamine in the brain, which is what induces the motor symptoms associated with PD, motor symptoms of PD are largely treated by medications that increase the level of dopamine in the brain, thus improving the motor symptoms.[3] More difficult to treat, however, can be the nonmotor symptoms of PD like emotional dysregulation, sleep disturbances, and depression. Depression, which is very broad but described by the National Institute of Health as a serious mood disorder[3], in those who have PD can be difficult to treat and diagnose since normal depression symptoms like cognitive changes, sleep problems, and appetite disruption are also regular symptoms of PD, making it difficult to assess which symptoms are a result of which condition.[2] Within the population of people who have PD, higher rates of depressive symptoms are found. As PD involves the loss of dopaminergic, noradrenergic, and serotonergic neurons, all of which are involved in the regulation of mood and mood disturbances, neurobiological factors associated with PD explain the higher rates of depression found within the PD population.[2] Another potential explanation is that the loss of dopaminergic neurons leads to dysfunction in the brain, disrupting serotonergic neurons and the depression-related thalamic circuits within the brain.[2] Depression can, therefore, be brought on by the physiological event itself that causes PD, which is what makes PD depression distinctive from depression in those without PD. Thus, it would not be a foreign idea if the treatment of PD depression would be different or have slight modifications compared to the treatment of regular depression. Despite these distinctions, there still has not been enough treatment studies about PD depression. Regardless, patients with and without PD have the same form of depression treatment: antidepressants. Overall, the neurological complexities regarding depression in PD and its distinction from normal depression permit more investigation into treatments.

Music therapy is a treatment becoming more widely used and explored in other fields for a variety of uses. Music therapy is used as a nonpharmacological treatment for therapeutic purposes in medical contexts. The therapy can entail a variety of forms including dancing, singing, using instruments, walking to simple rhythms, and community music classes, with all of these forms ranging from simple to complex in their design. As music stimulates sensory areas of the brain like hearing and touch, it is no wonder that music's potential has been exploited for rehabilitative impact. Within the current research literature, music therapy and PD are two disparate topics that are slowly starting to conjoin together. Even though music therapy is also currently being researched as a motor symptom treatment in PD, the research into the emotional aspect is potentially promising, as there are currently not enough detailed focuses on PD depression.

3. Methodology

3.1 Literature Search

A literature review of English-language studies was conducted between January 25, 2019 to April 15, 2019 regarding the effect of antidepressant medication or music therapy on depression/mood in patients diagnosed with PD. Research was collected from the PubMed database through the VCU Library. Primary search terms were "emotional symptoms of Parkinson's disease," "music therapy in Parkinson's disease," "antidepressants in Parkinson's disease," and "depression Parkinson's disease."

Inclusionary criteria for this literature review required that articles were published in the 21st century, utilized pre- and post-patient-reported outcome measures to analyze effect on depression or mood, enrolled participants that were diagnosed with idiopathic Parkinson's disease, and specified antidepressant medication or music therapy treatment. If a meta-analysis was published in the 21st century, it was included even if the meta-analysis analyzed research that was also published in the 20th century. The absence of a pre- and post-patient-reported outcome measure was the most significant exclusionary criteria in studies sourced through PubMed. More inclusionary criteria were considered (e.g. that depression was formally diagnosed in accordance with NIH recommendations, that severity of depression was established, that the research be a depression treatment study only, etc.). However, the consideration of more criteria would have significantly limited the articles to be included in this paper. Given that depression was not formally diagnosed but rather assumed through score totals on patient-reported outcome measures, which are more accurately considered as screeners, the term "depression and mood" or "depression / mood" is utilized versus the term "depression" alone. A total of six articles were identified to be included in this literature review.[4-9]

There was only one reviewer for the articles (Emaan Dawood). Articles were reviewed weekly and statistical analysis was completed independently with guidance from professors and graduate students.

3.2 Statistical Analysis

Analysis was conducted from guidance of professors and graduate students. An online effect size calculator was utilized to confirm effect sizes that were calculated by hand.[10] The dependent measure was the effect size between baseline and post treatment measures of depression that was expressed in Cohen's *d*. A Cohen's *d* index is the difference in means between two groups and is expressed in standard deviation units. Therefore, *d* is expressed as the change in baseline. Understanding the effect size in terms of its standard deviation units allows one to understand the magnitude of change or effect. A *d* equaling .2 is considered a small effect size, *d* equaling 0.5 is considered a medium effect size, and *d* equaling 0.8 is considered a large effect size. If the means of two groups differ by less than 0.2, the difference is considered trivial despite statistical significance. Cohen's *d* was derived by
subtracting the mean baseline depression score (M_2) from the mean follow up depression score (M_1) and divided by the pooled standard deviation (SD_{pooled}).

$$\text{Cohen's d} = (M_2 - M_1) / SD_{pooled}$$

$$SD_{pooled} = \sqrt{((SD_1^2 + SD_2^2)/2)}$$

4. Results

4.1 Publication Date

Between January 1, 2000 and April 15, 2019, a total of six studies were identified that met inclusion criteria. The examined time frame was 19 years.

4.2 Study Design

Excluding the meta-analysis included in the review, less than a quarter (1/5, 20%) of the studies measured effect of antidepressant medication in mood and depression in patients with PD[5], and greater than half (4/5, 80%) of the studies measured effect of music therapy in mood and depression in patients with PD.[6-9] Including the meta-analysis, which focused solely on the effect of antidepressant medication in depression in patients with PD and analyzed twenty-seven articles, greater than half (28/32, 87.5%) of the studies focused on change in depression in individuals with PD.[4,5]

Excluding the meta-analysis, more than half of the studies focused primarily on depression and mood (3/5, 60%)[5,7,8], while less than half (2/5, 40%) focused secondarily on depression and mood.[6,9] Including the meta-analysis, greater than half of the studies focused primarily on depression and mood (20/32, 62.5%)[4, 5, 7, 8], and less than a half (12/32, 37.5%) focused secondarily on depression and mood.[4, 6, 9]

One study was a meta-analysis[4], one was a multi-center randomized control trial[5], one was a single center randomized control trial[8], one was a controlled prospective and cohort trial[6], and two were pilot studies.[7,9] All studies provided specified trial duration with specified antidepressant medication types or music therapy protocols.

4.3 Sample Size

Including the meta-analysis, 757 subjects completed the studies. Excluding the meta-analysis, 89 subjects completed the studies.[5-9] The mean study sample size, excluding the meta-analysis, was 17.8 (range = 8 - 39). For the meta-analysis, which focused on antidepressant treatment only, the mean sample size was 28.6 (range, 8 - 93).[4]

4.4 Inclusion Criteria

Excluding articles in the meta-analysis, all (5/5, 100%) articles were published in the 21st century, provided pre- and post-patient reported outcome measures related to depression, enrolled the idiopathic Parkinson's disease population only, and specified the antidepressant medication type or music therapy protocol.[5-9] Excluding the meta-analysis, no studies utilized a formal diagnostic criteria to define depression (e.g. from the DSM-V criteria) and no studies specified severity levels, though the range for the average severity of the sample could be extrapolated based on the mean and standard deviation of the patient-reported outcome measures.[5-9] Excluding the meta-analysis, less than half (2/5, 40%) included participants with depression severity ratings mild to severe according to the patient reported outcome measures from [5, 8], and greater than half (3/5, 60%) included participants from normal to mild according to the patient reported outcome measures.[6, 7, 9]

Including the meta-analysis, less than half (14/32, 44%) the articles were published in the 21st century[4] and most (27/32, 84%) utilized pre- and post-patient reported outcome measures related to depression.[4-9] Less than half (13/32, 41%) utilized formal diagnostic criteria to define depression[4], and roughly a third (10/32, 31%) specified severity levels.[4]

4.5 Outcome Measures

Including the meta-analysis, researchers utilized a variety of patient-reported outcome measures. Thirteen utilized the Hamilton Depression Rating Scale[4], four the Zung Scale[4], three the Montgomery Asberg Rating Scale (MADRS)[4,9], two for the Geriatric Depression Scale (GDS)[6,7], two for the Parkinson's Disease Questionnaire-39 (PDQ-39)[7,8], and one each for the Anderson Scale[4], Beck Depression Inventory[4], Profile of Mood States[4], Happiness Measure (HM)[8], Apathy Scale[5], Parkinson's Disease Quality of Life Questionnaire (PDQL)[8], and Quick Inventory of Depressive Symptomatology-Japanese version (QIDS-J).[5]

4.6 Statistical and Qualitative Analysis

4.6.1 analysis of treatment effects

For the meta-analysis study, the effect size for Cohen's *d* equaled 0.95 for both active medication treatment and placebo conditions.[4] For the randomized control study for antidepressant medication, a Cohen's *d* effect size for antidepressant treatment with serotonin and norepinephrine reuptake inhibitors (SNRIs) was 0.6 and 0.31 on the QIDS-J and Apathy Scale, respectively, at the conclusion of the study.[5] For this same study, a Cohen's *d* effect size

for antidepressant treatment with selective serotonin reuptake inhibitor (SSRIs) was found to be 0.57 and 0.4 on the QIDS-J and Apathy Scale, respectively, at the conclusion of the study.[5] The controlled prospective and cohort trial study that analyzed the benefit of a singing program on voice quality for patients with PD but collected secondary measures on mood via the GDS determined the Cohen's *d* effect size to be 0.65 at conclusion of treatment and 0.34 at the 6-month follow up.[6] The twelve week pilot study analyzed the benefit of drumming on mood for patients with depression and PD and found the Cohen's *d* effect size to be 0.3 and 0 as measured by the GDS immediately at conclusion of the study and at a 12 week follow up, respectively.[7] Though this study had a control group, the Cohen's *d* effect size could not be calculated due to missing data. A single blinded, randomized controlled study looked at the benefit of a specific music therapy protocol on depression in individuals with PD and found the Cohen's *d* effect size to be 2.59 and 0.31 measured by the Happiness Measure immediately after treatment and at two months follow up, respectively.[8] This same study found the Cohen's *d* effect size for this group to be 5.69 and 0.19 measured by the PDQL immediately after treatment and at two months follow up, respectively. This same study enrolled patients with low mood/depression and PD into a controlled group receiving physical therapy as treatment. The Cohen's *d* effect size for this group was 0.19 and 0.24 measured by the Happiness Measure immediately after treatment and at two months follow up, respectively. For the control group, the Cohen's *d* effect size, as measured by the PDQL, was found to be 0.3 and 0.25 immediately after treatment and at two months follow up, respectively.[8] The other pilot study in this literature review studied the effect of group music therapy on primarily voice and speech but collected data on changes in mood as a secondary measure via the MADRS and found the Cohen's *d* effect size to be 0 immediately at conclusion of the study.[9]

4.6.2 qualitative analysis

The pilot study analyzing the effect of drumming on mood and depression in patients diagnosed with PD and the study analyzing the effect of a singing therapy protocol provided qualitative data regarding the benefit of such therapies on mood. Participants reported improvements in feelings of isolation and improved socialization in both studies.[6-7]

5. Discussion

The results demonstrated that for antidepressant medication treatment studies, there was a mix of medium and high effect size indicating variation in how mood/depression improved from baseline. In the meta-analysis, it is also interesting to see that placebo had a similarly high effect size as the antidepressant medication on mood and depression. The meta-analysis did not further explain how this may have occurred but further studies into placebo effect for mood disorders within this population may be warranted.

Music therapy studies demonstrated even greater variation in effect size ranging from no effect to very high effect sizes. The results also consistently demonstrated that any positive effect that the music therapy treatment may have had on a participant's mood or depression reduced over time, indicating that treatment effects are perhaps not long lasting. It is also notable to point out that the study that focused on a general music therapy (MT) program with mood/depression as a primary measure[8] had a significantly high effect size (i.e. 2.59 and 5.69) whereas the drumming therapy program that focused on mood and depression as a primary measure[7] had a relatively lower effect size (i.e. 0.3 and 0). This effect size difference is most likely accounted for by the fact that the general MT program enrolled patients with possible mood disorder severity ratings ranging from normal to severe[8], whereas the drumming therapy program enrolled patients with possible mood disorder severity ratings ranging from normal to mild[7], naturally resulting in a lower effect size. This explanation for variation in effect size can be generalized to all four music therapy studies in this literature review.

For all studies analyzed in this paper, variation in effect size can also be accounted for by: small sample sizes that increase likelihood of error; use of different patient-reported outcome measures where some measures are perhaps more sensitive to change than others; different treatment protocols for both antidepressant medication treatment and music therapy programs; and study focus with mood and depression being secondary versus primary measures.

Given this variation and that antidepressants are currently the standard form of depression treatment in PD, more research must be put into improving antidepressant design, as effective treatment for depression in PD is important. The further development of music therapy and antidepressant research within the context of PD depression could make comparisons meaningful. At this time, concluding that one treatment type is better than the other is not feasible, as the studies concerning music therapy and antidepressants in PD depression are limited and largely inconclusive.

To improve research within the area of treating depression in those with PD, a variety of aspects need to be addressed. Studies analyzing the effect of depression in PD patients must utilize the same formal, standard method of diagnosis for depression with the standardized methods for severity ratings. Research in this area must also prioritize determining which patient-reported outcome measures are the most valid, reliable, and sensitive to change. Once this is determined, researchers must strive to utilize the same outcome measures so as to create more reliable methods of comparison across studies. It is also recommended that studies strive to increase sample size for improved statistical power, formulate controls for added comparisons, and focus primarily on depression versus motoric characteristics with depression as a primary measure. Research in this area should also continue to report qualitative analysis as qualitative data may possibly reveal information that the quantitative data cannot capture. For example, one such participant in the singing therapy study that did not have large improvement in GDS scores said, "I feel good because I can look back on my happy childhood when I sing the songs from that time, despite the fact that I am getting older with incurable disease" after their sessions. The effect size for this study was considered low yet the qualitative data revealed a positive outcome that the quantitative data did not reflect.[6]

Given the potential seen in PD music therapy studies, a future research project examining the two specific treatment types using the same patient-reported outcome measure could be more revealing. In such a study, the best recommended antidepressant for PD depression should be compared to a specific type of music therapy, preferably the best and most developed one revealed by additional and replicated studies. Two groups of patients with PD with clinically significant depressive symptoms of a larger sample size would randomly be assigned to an antidepressant treatment group or a music therapy treatment group. The same depression rating scale should be used on both of these groups to measure their depression pre and post treatment. Hypothetical participants should be similar in demographics and environments as much as possible to minimize confounding factors. The depression rating scale that could be used for both groups is the GDS, one of the more widely used patient-reported outcome measures for evaluating depression in people who have PD. The GDS scores of both groups pre and post treatment would reveal how well each treatment worked, and the amount of change in GDS scores for each treatment and its effect size would help compare the treatments. Such a type of experiment can be modifiable to the type of antidepressant or music therapy and group of PD patients being used. This more controlled study with the intention of comparing antidepressants to music therapy could be more clarifying in answering such a question, and such research could reveal if music therapy can become a more widely implemented form of depression treatment in PD.

One of the crucial elements of managing the health of patients with PD is treating their depression, especially given the high rates of depressive symptoms within the PD population. The complex distinctions between depression in people who have PD and in people without PD make its treatment even more important but also more difficult. The current and most common form of PD depression treatment is antidepressants, despite the limiting amount of antidepressant treatment studies on subjects with PD, the lack of consistent results, and side-effects. Therefore, PD depression treatment methods need to continue to be further developed and explored. The potential benefits of music therapy increase the need for more research into music therapy using controlled environments and larger sample sizes if possible, and such research with antidepressants is equally important. While further and better research is conducted into antidepressant and music therapy use in PD, other research can also be conducted into specifically and intentionally comparing antidepressants and music therapy to better reveal if one is better than the other and if music therapy could potentially replace antidepressants. Until that research is obtained with consistent results, music therapy could be used as a supplement to antidepressants for treating depression in PD given that music therapy can provide connections to others and physical activity, which is understood to help improve mood. Finding the best possible treatment for depression in PD will be tough but can be accomplished through diligence and thorough investigation of all treatment options.

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