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Comparison of Selective Serotonin Reuptake Inhibitor Monotherapy and Dual Therapy with Physical Exercise in Mood Disorders

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by

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Introduction

It is well known that exercise is an underutilized part of medical care and counseling that is recommended to patients. It is also estimated that roughly 21.4% of the general population will experience a mood disorder in their lifetime (Kessler, 2005). These two components together indicate a strong need to determine the effect that exercise will have on a significant patient population that is encountered in the primary care setting. The purpose of this paper is to look at the comprehensive amount of literature regarding exercise and Selective Serotonin Reuptake Inhibitor (SSRI) therapies in patients with mood disorders to determine if dual therapy is better than a monotherapy SSRI regimen. By looking at this information, the determination can be made of how important consistent weekly exercise routines are in patients with mood disorders and better enhance the quality of life in these patients.

Statement of the Problem

The *Diagnostic and Statistical Manual of Mental Disorders V (DSM-V)* breaks mood disorders into two distinct groups: depressive disorders and bipolar disorders. Depression and other mood disorders make up a large part of common clinical practice with almost 10% of family medicine patients having depression or a related condition annotated in their medical chart according to the CDC. This presents an enormous burden on healthcare providers with regards to management of these patients and creates a need for a versatile approach to treat these individuals. Many individuals who suffer from mood disorders are required to be on lifelong medication and sometimes where one medication is not effective enough patients have to deal with added burden of polypharmacy with multiple medications. It is possible that by adding exercise to a treatment regimen patients can reduce their polypharmacy for their condition or eliminate pharmaceutical therapy all together.

Research Question

Does a dual therapy regimen of consistent resistance or aerobic exercise along with an SSRI regimen yield lower instances or severity of symptoms in patients with mood disorders versus a monotherapy regimen of SSRI medication?

Methods

A comprehensive literature review was performed using electronic search databases, including PubMed, CINAHL, AccessMedicine, and Clinical Key. Searches of articles included the keywords SSRI monotherapy, dual therapy, and exercise for mood disorders. The articles searched were limited to the past 20 years to ensure all information was relatively current. The literature review yielded a total of over 3,600 results. Exclusion criteria included periodicals, editorials, and books to eliminate any non-research pieces. The types of studies included were randomized controlled trials, meta-analysis, clinical trial, and systematic reviews. After removing research articles that met the exclusion criteria, 11 studies met all parameters set and were thus used in this comprehensive literature review.

Literature Review

A review of the literature shows that the bulk of the research that has been completed regarding exercise and mood disorders has been on individuals who are suffering from depression. There were only a few examples of work that had been conducted on individuals who suffer from anxiety, bipolar disorder, or any other mood disorders. On the topic of depression, however, and more specifically late life depression, an extensive amount of research has been conducted that shows exercise when combined with an SSRI greatly reduces the severity of symptoms. This is encouraging to see that there is evidence to indicate dual therapy is more effective for depression

would be helpful but also, opens the door for new research to be conducted on individuals with other mood disorders.

Efficacy of Exercise as a Therapy for Mood Disorders

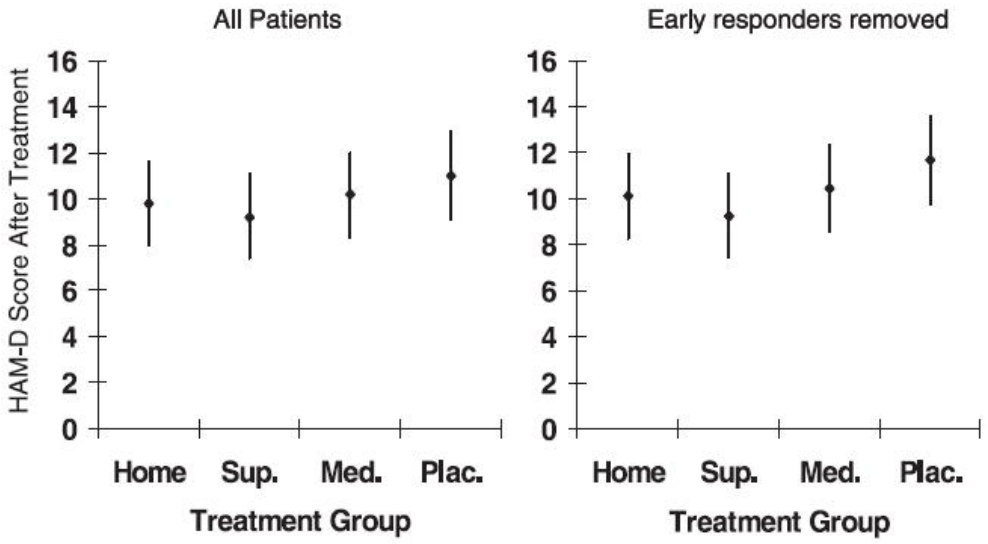
Blumenthal et al (2007) published a study that evaluated the effect of exercise versus Selective Serotonin Reuptake Inhibitor (SSRI) therapy, as well as a placebo group in individuals that were affected with major depressive disorder. The study, conducted between 2000 and 2005, consisted of 202 adults of which 153 were women and 49 were men. The participants of the study were subjected to a randomized control trial and were considered part of the SMILE study, which was a large prospective cohort study, focusing on different aspects of disease, health and lifestyle of people living in Eindhoven, the Netherlands. Eindhoven is a city in the Southern part of the Netherlands of approximately 200,000 inhabitants. The participants of the Blumenthal study were divided into four groups that would be evaluated over a course of 16 weeks. The four categories of the study were group exercise, home exercise, a prescription of sertraline 50-200mg by mouth daily, or a placebo.

The participants of the study that were prescribed the placebo or the sertraline (SSRI) were monitored via pill count at two, four, eight, 12, and 16 weeks. The participants who were placed on exercise routines, as well as the participants who were using medication, were evaluated by a psychologist that was blinded to the treatment that the patient was on at the same weekly markers to monitor progress. To make the initial diagnosis of major depressive disorder (MDD) and monitor progress in the program, the 17-item Hamilton Depression Rating Scale (HAM-D) was used to assess MDD severity at baseline and after 16 weeks. Patients were also monitored for their safety and to rule out suicidality by using a Beck Depression Inventory II list via a telephone consult weekly for the first four weeks and then biweekly afterwards until the 16-week mark.

The results of the data were compiled and subjected to generalized linear models with maximum likelihood estimation available in PROC GENMOD software program that is provided by the organization SAS using the version 9.1. The results showed that after four months of treatment, 41% of the participants achieved remission, defined as no longer meeting the criteria for major depressive disorder (MDD) and a HAM-D score of <8. Patients receiving active treatments had higher remission rates than the placebo controls: supervised exercise = 45%; home-based exercise = 40%; medication = 47%; placebo = 31% (p = .057) The results, which can also be seen in figure 1, support the hypothesis that a regimented exercise program could be as effective, within reason, as a beginning prescription of sertraline for the treatment of MDD.

Figure 1

HAM-D results of participants after treatment



Note: Abbreviations for the categories are as follows Home = Home exercise, Sup. = Supervised exercise, Med. = Medication alone, and Pac. = Placebo. The data for figure 1 was retrieved from “Exercise and pharmacotherapy in the treatment of major depressive disorder.” Blumenthal JA, Babyak MA, Doraiswamy PM, Watkins L, Hoffman BM, Barbour KA, Herman

S, Craighead WE, Brosse AL, Waugh R, Hinderliter A, Sherwood A. Published online 2007 Sep 10

The study that was completed consisted mostly of (75%) women, which is not as valid as a study that consists equally of both of genders. Another drawback of the study is that, while adherence was being monitored for the group exercise portion, it was almost impossible to truly ensure that the home exercise group was completing the regiment; this could lead to inaccurate data. The third drawback of the study is that most participants (90%) had a college background and resided in one particular part of the Netherlands and therefore the study is limited to a particular demographic of individuals, who might have had more access to resources than what would be considered a more inclusive model over all socio-economic backgrounds.

Miser (2000) published a study that was similar to Blumenthal, however, it focused primarily on older patients between the ages of 50 to 77 years old. This study included a total number of 156 participants. After an initial assessment, in which the HAM-D assessment form was used by clinical psychologists, eligible subjects were randomized to exercise (supervised group aerobics consisting of walking or jogging for 30 minutes three times a week at an intensity to achieve 70% to 85% of maximum heart rate); antidepressant (SSRI) therapy (sertraline 50 mg titrated up to 200 mg a day as needed to achieve effectiveness); or a combination of exercise and antidepressants. The participants were evaluated by the HAM-D and the Beck Depression Inventory at weeks one, two, three, four, six, eight, and twelve to evaluate both their overall safety and to ensure there was no suicidality among the participants. When the trial came to an end, between 60 – 69% of the participants were no longer depressed using the HAM-D questionnaire. In this study, there was no statistically significant difference between the groups that participated in exercise and those that were given the prescription of sertraline.

This study had several drawbacks. The first of which is that a true statistical analysis was not completed using a linear regression. This makes the data easier to misconstrue or to be worked in a way that is beneficial. This study also lacked a placebo group, so we can not determine if exercise alone had an effect on the participants' MDD. The author of the study also notes that it is difficult to determine the percentage of patients who had mild or more severe depression. The average HAM-D score was 18, however, it appears that most had mild depression. It is possible that had the participants of the study had more severe MDD, the responses to the three categories may have been completely different.

Overall, meta-analyses are lacking on the topic of exercise and its effect on mood disorders. However, Nieuwenhuijsen et al (2020) did complete a comprehensive analysis regarding workplace intervention impact on individuals with major depressive disorder with regards to sick days taken throughout the year. Work intervention can be defined as workplace changes, whether it be a different routine, taking more breaks during work, or changing an individual's duties. Workplace intervention was compared to other categories, such as medication therapy in the form of SSRI and SNRI prescriptions, cognitive behavioral therapy, and exercise and diet.

The meta-analyses looked at the combined work of 45 studies with 88 study arms, involving 12,109 participants with either a major depressive disorder or a high level of depressive symptoms. The studies were graded and standardized based on mean differences (SMDs) or risk ratios (RR) with 95% confidence intervals (CI) to pool study results. The study utilized only randomized controlled trials (RCTs) and cluster-RCTs of work-directed and clinical interventions for people with depression that included days of sickness absence or being off work as an outcome.

The results of the analysis showed that a combination of work-directed and concurrent clinical intervention reduces sickness absence days within the first year of follow-up, with a standard mean deviation (SMD) of -0.25, while having 95% confidence interval (CI) -0.38 to -0.12. This evidence was gathered using nine studies and translated into moderate certainty evidence. With regards to exercise regimens, the study showed that supervised strength exercise may reduce sickness absence, compared to relaxation with the (SMD) being -1.11 while having a 95% CI -1.68 to -0.54. This information was obtained by reviewing only one study and therefore, lead to a low amount of confidence. This analysis also had some limitations; the first of which was the studies involved typically did not involve a placebo group. Secondly, most of the studies reviewed by this group took place in Europe and not in the United States. Lastly/Finally, only individuals who are employed were involved and not those who suffer from mood disorders that are unemployed, retired, or in a student setting.

Dual Therapy SSRI and Exercise Usage Results

Micheli et al (2018) studied the neurological effects that both fluoxetine (SSRI) and running may have on individuals with depression. The basis for this study is that the effect of treatments for mood disorders can be observed looking at two specific neurogenic areas of the brain: the dentate gyrus of the hippocampus and the subventricular zone (SVZ) adjacent to lateral ventricles. More specifically, both fluoxetine and running can initiate neurogenesis in these areas and have a dramatic effect on individuals with depression. (Kemppermann, et al 2015) The study does an excellent job providing evidence for examining these regions of the brain to determine effects of treatments that are used for mood disorders such as depression. The authors found that Btg1-null mitotic stem cells increased significantly by running or fluoxetine compared to the control stem cells (about three-fold and 40% higher, respectively); this clearly indicates

how stem cells are endowed with a reserve potential which under specific conditions is revealed. In fact, the activation of neurogenesis after the end of the running exercise persists in Btg1-null dentate gyrus longer than in controls (3 months versus one month).

This study has one major limitation: only structural changes in stem cell lines with regards to specific structures in the brain were studied, but not clinical presentation of individuals suffering from depression. This of course, weakens the study in that the effects that are seen from both running and fluoxetine are structural based only and therefore are not being translated into actual decreased symptoms in potential patients.

In the study that was completed by Hoffman et al (2010), 202 sedentary adults with MDD were randomized to: a) supervised exercise; b) home-based exercise; c) sertraline (SSRI); or d) placebo pill. The authors reported the initial findings and further, completed a follow up exam at 1 year past the original 16-week mark of the original study. The authors examined two outcomes measured at 1-year follow-up (i.e., 16 months post randomization): 1) continuous Hamilton Depression Rating Scale score; and 2) MDD status (depressed; partial remission; full remission) in 172 available participants (85% of the original cohort).

Hoffman et al (2010) reported that at the time of the 1-year follow-up, rates of MDD remission increased from 46% at post treatment to 66% for participants available for follow-up. The authors documented that one limitation to the study was missing data because 15% of the original cohort of 202 participants were unable to be contacted for follow up. AAn unexpected finding was the absence of an association between antidepressant use at the time of follow-up and MDD remission. The authors justified that these participants were more likely to be treatment resistant but were, nevertheless, motivated to use antidepressant medications to reduce their depressive symptoms.

Efficacy of Dual Pharmacotherapy

Stewart et al (2014) examined the efficacy of multiple pharmacological agents on patients with MDD. To accomplish this task, 245 outpatients aged 18–65 having non-psychotic, non-bipolar major depression were randomly assigned to double-blind treatment with bupropion (atypical antidepressant) or escitalopram (SSRI), or the combination dosed to a maximum of bupropion 450 mg/d and/or escitalopram 40 mg/d for 12 weeks. A Montgomery–Asberg Depression Rating Scale score of 22 was required for randomization, while a Hamilton Rating Scale for Depression score ≤ 7 defined remission.

This study was based on previous work that had been completed by Blier et al (2010), where 105 patients DSM-IV criteria for major depressive disorder were randomly assigned to receive either fluoxetine (SSRI) monotherapy or mirtazapine (atypical antidepressant) in combination with fluoxetine, venlafaxine (SNRI), or bupropion (atypical antidepressant) for 6 weeks. This showed patients produce a more rapid improvement on combination therapy when compared to fluoxetine alone.

In contrast, Stewart et al (2014) reported that time to remission was not earlier in the dual therapy group than in the escitalopram (SSRI) group (Wald = .003, p = .960) or than in the bupropion (atypical antidepressant) group (Wald = 1.281, p = .258). The authors also reported that for both the HAM-D17 and the QIDS-SR-16, neither the comparison of dual therapy with escitalopram monotherapy nor with bupropion monotherapy was significant.

Stewart et al (2014) offers some insight as to why the findings of the study did not match the findings of the novel study including the possibility of an inappropriate population. The authors specifically mention that it is a possibility that Hispanics have an illness for which the study hypotheses do not apply. There seems to be more practical answers for the discrepancy in

the findings. Some of answers include that the study used escitalopram and bupropion compared to Blier et al (2010) used fluoxetine monotherapy or mirtazapine in combination with fluoxetine, venlafaxine, or bupropion. Since escitalopram is used more as a therapy for depression with anxiety symptoms, it may not be as effective at treating MDD as some of the other SSRI's that had been used in the novel studies.

Dual Therapy Involving Exercise vs Monotherapy

Siqueria et al (2016) was able to show that patients who participate in a four week aerobic exercise program of at least 20-60 minutes of exercise four times weekly are able to use a lower dosage of a SSRI regimen compared to those who do not. In order to accomplish this task, the authors followed 57 patients (18–55 years of age) for 28 days. All patients were drug-free, had been diagnosed with symptomatic MDD, and received flexible dose of sertraline (SSRI) during the trial. Patients were randomized to either a four week program (4x/week) of add-on aerobic exercise (exercise group, N = 29) or no activity (control group, N = 28). Depression severity was assessed using the Hamilton Rating Scale for Depression (HAM-D) as the primary outcome. The primary outcome measure was the severity of depressive symptoms, as determined by the HAM-D scores. Secondary outcome measures were overall physical fitness and cardiac function and association with antidepressant response.

The results of the study, which can be seen in table 1, showed that the changes in the HAM-D and BDI scores, even when considered both groups, were still not sufficiently significant to represent an association between a regular program of exercise and a reduction in the severity of depressive symptoms. However, the authors showed a marked decrease in HAM-

D scores with a lower dose of SSRI therapy. Specifically, 15 out of 29 individuals in the group with exercise required only 50mg of sertraline while the control group required 100mg of sertraline at the end of the study. This raises the need for further study on the topic to determine if exercise can serve as a suitable adjunct and means to reduce the overall dose of an SSRI in patients who are suffering from MDD.

Table 1

Socio-demographic and medical characteristics in the exercise group and controls.

	Exercise (n = 29)	**Control (n = 28)**	***p*-value***
Age (years)- *mean (SD)*	39.76±11.60	37.86±9.85	0.506
Gender-n (%)			
- Female	21 (72.4%)	20 (71.0%)	0.9
- Male	8 (27.6%)	8 (29.0%)	
Education on Set- *n (%)*			
- Low	0 (0.0%)	6 (21.5%)	0.955
- Intermediate	11 (38.0%)	9 (32.1%)	
- High	18 (62.0%)	13 (46.4%)	
Smoker- *n (%)*			
- No	21 (72.4%)	26 (92.9%)	0.9
- Yes	8 (27.6%)	2 (7.1%)	

	Exercise (n = 29)	**Control (n = 28)**	***p*-value***
Professional status- *n (%)*			
- Employed	23 (79.4%)	24 (85.7%)	0.97
- Unemployed	1 (3.4%)	1 (3.6%)	
- Student	5 (17.2%)	3 (10.7%)	
Duration of illness- *mean (SD)*	53.89±64.16	51.64±64.12	0.846
Final dose of the antidepressant- **n (%)**			
- 50 mg	15 (52%)	5 (18%)	0.01
- 100 mg	5 (17%)	15 (54%)	
- without medicine	9 (31%)	8 (28%)	

Note: Table 1 was retrieved from "Antidepressant Efficacy of Adjunctive Aerobic Activity and Associated Biomarkers in Major Depression: A 4-Week, Randomized, Single-Blind, Controlled Clinical Trial" Siqueira CC, Valiengo LL, Carvalho AF, Santos-Silva PR, Missio G, de Sousa RT, Di Natale G, Gattaz WF, Moreno RA, Machado-Vieira R Electronically Published 2016 May 6

The weaknesses that are in the study conducted by Siqueria Et Al can be evaluated by noting three different characteristics of the study. The first of which is that the study had a relatively small sample size;there were 47 participants spread across a wide age gap. This makes it difficult to establish substantial trends in the data. The second weakness of this study is that the exercise program only lasted four weeks. It is certainly reasonable to hypothesize that, had the

exercise program continued for a longer period, it would have yielded more statistically significant results. The third weakness of the study is that an add on design was used regarding the antidepressant, compared to other studies have used a titrated dose of an SSRI over a longer period. One could hypothesize that with a titrated dose over a period of 12-16 weeks, the combined effect with the exercise would have yielded different results.

Studies on juvenile individuals with mood disorders are lacking due to the ethical implications involved with working on younger patients. However, mood disorders are affecting younger patients at alarming rates. Schoeman et al (2017) attempted to look at the effect that exercise could have on younger patients with mood disorders by applying research to a rodent model. In the study Schoeman et al (2017) conducted, the authors investigated the effects of fluoxetine (SSRI) with and without exercise at postnatal day 35 (PND35) as well as PND60 to PND61 for long lasting effects and finally of pre-pubertal (PND21 to PND34) by examining bio-behavioral markers of depression and oxidative stress in stress sensitive Flinders Sensitive Line rats.

To complete the task, the authors of the study bred, supplied, and housed Male Flinders Sensitive Line (FSL; n = 179) and Flinders Resistant Line (FRL; n = 12). The FSL rats were sensitive to the biomarkers that are seen in depression and the FRL rats were resistant to the biomarkers, thus making the FRL rats the control group. The authors subjected the rats to low and moderate intensity exercise and either 5 mg/kg/day or 10 mg/kg/day of fluoxetine; they then measured biomarkers of depression (BDNF) and oxidative stress (lipid peroxidation, superoxide dismutase activity). The authors reported that low, but not moderate, intensity exercise or five, but not ten, mg/kg/day fluoxetine displayed anti-depressant-like properties at PND35. Pre-pubertal treatment with five mg/kg/day fluoxetine or low intensity exercise exerted lasting anti-

depressive-like effects into adulthood, whereas the combination of these two treatments did not. Based on these findings it is reasonable to suggest that regimented low intensity exercise conducted over a twenty-eight-day period of time would have antidepressant effects on pre-pubertal individuals but this has to be taken as conjecture as the study looked at effects in animal models and not humans.

The study conducted by Schoeman et al (2017) used a relatively small sample size of participants using an animal model; these two factors hinder the evidence that the study brought forth. However, the results showing that exercise can produce antidepressant effects in mammalian organisms is promising that exercise could also help human pre-pubertal individuals that suffer from mood disorders such as anxiety or MDD.

While data is lacking on younger individuals with mood disorders, there are multiple studies that examine the effects of exercise and SSRI therapy on older individuals. The first study that was examined within these parameters was the study that was conducted by Neviani et al (2017). Neviani et al (2017) analyzed data from the Safety and Efficacy of Exercise for Depression in Seniors (SEEDS) study. Neviani et al (2017) specifically focused on the cognitive abilities and disabilities that are associated with late life depression. The SEEDS study was a single-blind, randomized study that included 121 patients from four centers in the region of Emilia Romagna, Italy. A trial comparing the antidepressant effectiveness of sertraline (S) (SSRI) at a 50 mg dose against sertraline 50 mg plus three times weekly non-progressive exercise (S+NPE), and sertraline 50mg plus three times weekly progressive aerobic exercise (S+PAE). Exercise was conducted in small groups and monitored by heart rate meters. The groups met four times a week and exercised for 60 minutes during each setting. Patients with late-life depression without severe cognitive impairment were recruited from primary care and

assessed at baseline and 24 weeks, using the Montreal Cognitive Assessment (MOCA, total and subdomain scores) and Brief Disability Questionnaire. Analyses were based on Generalized Linear Models.

The authors of this study reported that progressive aerobic exercise combined with sertraline led to greater improvements of disability and cognition compared with sertraline alone, among elderly patients with major depression. More specifically, compared with the S group, patients in the S+PAE group displayed greater improvements of MOCA total scores (p=0.006, effect size=0.37), visuospatial/executive functions (p=0.001, effect size=0.13), and disability (p=0.02, effect size=−0.31). Participants in the S+NPE group did not display significant differences with the control group.

The authors themselves noted limitations with this study. The first limitation was the relatively small sample size that was included in the study. The second limitation was that the participants in the study were evaluated using the MOCA questionnaire, which isn't as reliable as a full neurological assessment to determine cognitive disabilities in the elderly. The authors also considered that socialization between the members in the group might have played a role in the decrease of symptoms. By meeting with other people and achieving a higher level of socialization, it is quite possible the members of the study were able to some obtain some benefit as they participated.

A second study was completed using the original data from the SEEDS study which was completed by Murri et al (2018). Murri et al (2018) focused efforts on which depressive symptoms exercise and SSRI combined therapy would address the most.

The methods of the study were similar to that in the study completed by Niviani et al (2017). The authors completed a secondary analysis of the information that was obtained in the

SEEDS study, however the authors looked exclusively at sertraline (S) (SSR) and sertraline plus exercise (S+EX). The authors did not distinguish aerobic progressive exercise and non-progressive exercise. The information was gathered from group exercise that was delivered three times weekly in small groups and monitored by heart rate meters. Patients with late life depression (n=121) were assessed at baseline, 4, 8, 12, and 24 weeks with the Hamilton Depression Scale. Scores of affective, vegetative, anxiety and agitation/insight factors were analyzed using Multilevel Growth Curve Models and sensitivity analyses (multiple imputation).

The authors of the study reported that compared with the S group, patients in the S+EX group displayed significantly greater improvements of the affective symptom dimension (total effect size = 0.79) with largest changes in the first four weeks and last 12 weeks. Improvements were mainly driven by depressed mood and psychomotor retardation. This information can also be observed in Table 2.

Table 2

Baseline characteristics of participants that participated in SEEDS study.

	S (n = 42)	S+EX (n = 79)	Statistics
Sociodemographic			
Age, mean (SD)	75.6 (5.6)	74.9 (6.2)	t = 0.39, p = 0.53
Gender, F (%)	76.2	68.4	χ^2 = 0.82, p = 0.37
Marital status, single (%)	54.8	54.4	χ^2 = 0.01, p = 0.97
Education, elementary or less (%)	64.3	48.1	χ^2 = 2.89, p = 0.09
Living alone (%)	45.2	44.3	χ^2 = 0.01, p = 0.92
Physical-medical			
BMI, mean (SD)	25.8 (3.3)	26.0 (3.8)	t = 0.07, p = 0.79
CIRS severity index, mean (SD)	1.31 (0.22)	1.40 (0.23)	t = 4.10, p = 0.05 *
CIRS comorbidity index, mean (SD)	0.57 (0.80)	1.26 (1.16)	t = 12.9, p = 0.001 *
Peak VO_2, mean (SD)	15.8 (2.7)	15.3 (3.6)	t = 0.32, p = 0.58
MOCA total score, mean (SD)	21.4 (4.2)	21.6 (4.1)	t = 0.03, p = 0.86

	S (n = 42)	S+EX (n = 79)	Statistics
Psychiatric-cognitive			
Brief Disability Questionnaire, mean (SD)	9.6 (4.3)	9.5 (4.5)	t = 0.16, p = 0.87
Onset of depression after 55 years, %	46.3	45.5	χ^2 = 0.01, p = 0.93
Treated with antidepressants lifetime (%)	73.8	64.6	χ^2 = 1.08, p = 0.30
>2 depressive episodes lifetime (%)	42.9	31.0	χ^2 = 1.45, p = 0.23
History of suicide attempt (%)	2.4	2.7	χ^2 = 0.01, p = 0.93
HAM-D total score, mean (SD)	20.4 (3.4)	20.0 (2.9)	t = 0.66, p = 0.42
Symptom dimension scores (HAM-D factors)			
Baseline			
Affective	1.25 (0.32)	1.25 (0.35)	t = 0.01, p = 0.99
Vegetative	0.96 (0.37)	0.85 (0.41)	t = 1.37, p = 0.17
Anxiety	1.75 (0.72)	1.73 (0.65)	t = 0.16, p = 0.88
Agitation/Insight	0.82 (0.56)	0.87 (0.56)	t = 0.49, p = 0.63
Study end			
Affective	0.63 (0.42)	0.43 (0.35)	t = 2.36, p = 0.02 *
Vegetative	0.46 (0.38)	0.28 (0.30)	t = 2.63, p = 0.01 *
Anxiety	1.00 (0.67)	0.74 (0.66)	t = 1.85, p = 0.06
Agitation/insight	0.52 (0.44)	0.46 (0.48)	t = 0.60, p = 0.55

Note. Table 2 was retrieved from “Physical exercise for late-life depression: Effects on symptom dimensions and time course” Murri MB, Ekkekakis P, Menchetti M, Neviani F, Trevisani F, Tedeschi S, Latessa PM, Nerozzi E, Ermini G, Zocchi D, Squatrito S, Toni G, Cabassi A, Neri M, Zanetidou S, Amore M Electronically published 2018 Apr 1

The p score of 0.02 and 0.01 for affective and vegetative symptoms, respectively, certainly indicated that sertraline and exercise had the greatest effect on depressed mood and slowed psychomotor skills of patients that participated in the study. The authors noted that the greatest amount of improvement that was seen was at the 4-week mark and the 24-week mark. The authors did note, however, there were limitations to the work that was completed. The first

limitation that was noted was the same that was noted by Niviani et al (2018), which is that the sample size was relatively small, and a larger group could have yielded different results. The second limitation that was noted was that the original SEEDS study lacked an exercise only arm of the study which would offer a control for the effect of exercise on late life depression by itself without the assistance of an SSRI.

Anticipated Results

With regards to dual therapy of exercise and an SSRI versus use of an SSRI alone, iis anticipated that patients who routinely use resistance or aerobic exercise as part of their treatment regimen for mood disorders will see a greater reduction in severity or instances of symptoms related to their mood disorder compared to the patients who do not. It is also anticipated that individuals who partake in exercise routines will require a smaller dosage of a SSRI therapy regiment for their mood disorders. Lastly, it is anticipated that future studies will show that individuals who exercise on a routine basis will have a lower instance of mood disorders compared to individuals who do not.

Applicability to Clinical Practice

With the information provided in the literature review, the medical provider will be able to make a more versatile and well-rounded treatment option for their patients who suffer from mood disorders, as well as provide an overall better outcome for their patients.

Often times, providers are halted in progress with their patients that are suffering from mood disorders by slowly examining the effects of one medication after the other and titrating dosages down before switching to another medication. This process can be tedious and disheartening for both the provider and the patient. The information in this literature review can help provide medical

professionals with another tool to try and assist a remission of symptoms in mood disorders for their patients as well as reduce polypharmacy for patients that are taking multiple medications for their mood disorders.

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