Auricular Acupressure on Depression and Anxiety in Mothers with Peripartum Depression

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AURICULAR ACUPRESSURE ON DEPRESSION AND ANXIETY IN MOTHERS
WITH PERIPARTUM DEPRESSION

A Thesis Presented to
The Faculty of the School of Medicine
Yale University

In Candidacy for the Degree of
Master of Medical Science

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ABSTRACT

Peripartum depression is a prevalent mental health disorder characterized by clinically significant depressive symptoms that can markedly impair maternal functioning, mother-infant bonding, and infant development. Current treatments for peripartum depression include pharmacotherapy and psychotherapy, but cost, time investment, and potential adverse effects limit their effectiveness. Auricular acupressure has been shown to improve a variety of conditions, however, there is a lack of application in peripartum depression. In this study, we propose to determine whether magnetic bead auricular acupressure reduces symptoms in mothers with peripartum depression. Using a randomized controlled trial, we will assign patients to either acupressure or sham acupressure groups and examine changes in depressive symptoms using the Hamilton Depression Rating Scale after 4 weeks of treatment. The results of this study will provide insight on the effectiveness of auricular acupressure and may ultimately expand treatment options for peripartum depression with a safe, cost-effective, and patient-acceptable intervention.
CHAPTER 1: INTRODUCTION

1.1 BACKGROUND

Childbirth can be one of the greatest moments in a parent’s life; however, this event can also bring forth fear, anxiety, and emotional distress that can impair family dynamics.¹ This is an especially challenging transition period for mothers, leaving them highly susceptible to psychiatric disorders² such as postpartum psychosis and peripartum depression (PPD), formerly known as postpartum depression³,⁴. Of the two, postpartum psychosis has a lower prevalence, affecting 1-2 per 1000 women; however, it is more serious and requires hospitalization.⁵,⁶ Symptoms include paranoia, delusions, hallucinations, disorientation, insomnia, and attempts to harm self or the newborn.⁶ Postpartum blues is a mild or transient period of depressive symptoms affecting 50-80% of all mothers, and includes symptoms of irritability, sadness, anxiety, excessive crying, sleep disturbances, and appetite changes.⁷ It does not typically interfere with maternal care of the baby and generally self-resolves within two weeks postdelivery, however, if unresolved can lead to PPD.⁷ PPD affects about 10-15% of all mothers, with prevalence rates ranging lower in high-income countries and higher in low- or middle-income countries.¹,⁸-¹⁰ Women who experience PPD generally develop symptoms during pregnancy or within the 4 weeks after delivery.¹¹ These symptoms are similar to those of postpartum blues and are often comorbid with anxiety, but are more intense, take longer to resolve, and require medication and/or behavioral therapy.¹²-¹⁴

The exact cause of PPD is not known but is likely multifactorial with contribution from biological factors including hormonal changes during pregnancy, genetics, and immune function, as well as environmental factors including stressful and emotional life
Several studies have shown that peripartum fluctuations in hormones such as allopregnanolone, a progesterone metabolite and a modulator of γ-aminobutyric acid (GABA) receptors, affect both anxiety and depression.\textsuperscript{16,17} A sudden decrease in allopregnanolone levels after childbirth may play a critical role in triggering PPD by altering the function of GABA receptors.\textsuperscript{15,18} Genetic factors also contribute to the pathophysiology of PPD with evidence from family and twin studies suggesting that PPD clusters in families.\textsuperscript{19} Genetic variants (single nucleotide polymorphisms) found on chromosome 1q21.3-q32.1 and 9p24.3-p22.3 and in Hemicentin-1, all appear to increase susceptibility to PPD.\textsuperscript{20} Lastly, it is possible that changes in immune function during the perinatal period may increase risk for PPD. Anti-inflammatory cytokines, responsible for immunosuppression, are elevated during pregnancy to help maintain pregnancy; however, after delivery, the immune system quickly becomes proinflammatory and remains so for several weeks.\textsuperscript{15} Compared to women without PPD, those with PPD appear to have different gene expression that is functionally related to immunity.\textsuperscript{21}

Several environmental risk factors have been identified and also contribute to the development of PPD. Results from a meta-analysis of more than 14,000 subjects showed the strongest predictors were depression or anxiety during pregnancy, stressful life events during pregnancy or in the early postpartum period, low levels of social support, and a previous history of depression.\textsuperscript{10} Additional risks include a lack of financial support, poor marital relationship quality, history of anxiety, impaired infant-mother interactions, labor complications, low self-esteem, low educational level, unplanned or unwanted pregnancy, and adverse life events.\textsuperscript{10,11,22,23} Many of the risk factors for PPD fall under the umbrella of stress, and there is even a significant association between stressful life
events and the severity of depressive symptoms. In one study, women who experienced multiple adverse life events, including childhood or adulthood sexual abuse, were three times more likely to have PPD compared to those who did not experience any adverse life event. Additionally, a meta-analysis by Liu et al. (2022) showed that having gestational diabetes mellitus significantly increased the risk of PPD, highlighting the interplay between physical and mental health. Probable explanations for this relationship include not only the effect of hyperglycemia and hormones on the thyroid and stress axis, but the response to the stress burden of chronic diseases during the peripartum period.

The Diagnostic and Statistical Manual of Mental Disorders (DSM) categorizes PPD as a subtype of major depression and was previously listed in the DSM-IV as “Major Depressive Disorder, with postpartum onset.” However, given that as many as 50% of mothers with PPD have symptoms that begin during pregnancy, it is now listed in the DSM-V as “Major Depressive Disorder, with peripartum onset.” Diagnosis of PPD requires at least five of the following symptoms to be present during the same two-week period and must be a change from previous functioning: depressed mood, diminished interest or pleasure in activities, change in body weight (more than 5% in one month), sleep and appetite disturbances, psychomotor changes, fatigue or loss of energy, feelings of worthlessness or disproportionate guilt, decreased ability to concentrate, or suicidal ideation. Symptoms must be causing clinically significant distress or impaired functioning in life that is not due to psychoactive substances or other medical conditions. Although the DSM-V states symptom onset for PPD is during pregnancy or
within the four weeks following delivery, in the realm of clinical practice and research, the timeframe for PPD is variably defined from 4 weeks to 12 months after childbirth.\textsuperscript{29}

PPD is not only detrimental to the mother’s mental and physical health, but it can also adversely affect the partner, their relationship, the newborn, and any other children in the household.\textsuperscript{15, 30} Mothers with PPD are less likely to breastfeed, attend well-child visits, complete infant immunizations, and follow recommended safety practices such as usage of car seats or placing the infant on their back to sleep.\textsuperscript{31, 32} Impaired maternal mental health can affect infants in numerous ways, including poor (less secure) infant-mother attachment, an increased risk for gastrointestinal and lower respiratory tract infections, poor infant growth, impaired cognitive development, emotional maladjustment, and behavioral problems.\textsuperscript{33-37} Partners of mothers with PPD are also impacted, with increased partner depression and parenting stress.\textsuperscript{29} Furthermore, treatment studies have shown that those with untreated PPD are at risk for more weight problems, illicit drug use, social/relationship impairments, or persistent depression compared to those treated for PPD.\textsuperscript{38}

Treatment for PPD includes psychotherapy for mild-to-moderate cases and medication, such as antidepressants, for moderate-to-severe cases.\textsuperscript{1, 15} Selective serotonin reuptake inhibitors (SSRIs) are a typical first-line treatment\textsuperscript{15, 39}; however, there can be poor medication compliance due to side effects such as dizziness, inattention, and ataxia.\textsuperscript{40} Breastfeeding mothers are also hesitant to take medication since many of the drugs can make its way to the baby through the breastmilk.\textsuperscript{41-43} Even non-breastfeeding mothers report reluctance in taking medications due to the subjective perception of an excessive sedation causing them to not hear the baby at night and for the fear of potential
Additionally, these medications often take up to several weeks to become beneficial.\textsuperscript{45} Randomized clinical trials have shown mixed results and minimal evidence of superiority of antidepressants over their control groups for the treatment of PPD. Two systematic reviews also claimed that there is a lack of evidence from clinical trials to make a firm recommendation for the use of antidepressants.\textsuperscript{46, 47} Moreover, the U.S. Preventative Services Task Force has made no recommendation for the use of antidepressants.\textsuperscript{48}

Psychotherapy is an effective non-pharmacologic treatment option for PPD and includes cognitive behavioral therapy (CBT) and interpersonal psychotherapy (IPT).\textsuperscript{15} Patients undergoing CBT are encouraged to identify and change harmful patterns of thoughts, while those receiving IPT aim to contextualize depression within their relationships, expand interpersonal functioning, and increase social support.\textsuperscript{45} Benefits have been exhibited both in immediate post-treatment and long-term follow up (six months after the end of treatment); however, a lack of providers, cost, time constraints, lack of childcare, and concerns with stigma represent significant barriers to treatment access.\textsuperscript{49, 50} For these reasons, alternative therapies must be explored for the treatment of PPD.

Complementary and alternative medicine therapies are increasingly being sought out by patients with psychiatric disorders, including mothers with PPD.\textsuperscript{51, 52} These therapies refer to treatments that are not considered standard practices in western medicine and are used for health promotion, disease prevention, and illness treatment.\textsuperscript{51} One-fifth of pregnant women use complementary and alternative medicine for pregnancy related issues and report preference for these treatments due to a desire for a natural
approach, alignment with their personal beliefs, and previous challenges with traditional treatments.\textsuperscript{53-55} Complementary and alternative medicine can involve mind/body approaches such as physical activities or medicinal approaches with herbal treatments and vitamins.\textsuperscript{51, 52, 56} Some of the many complementary and alternative medicine therapies for perinatal depression include omega-3 fatty acids, St. John’s Wort, bright light therapy, exercise, massage, yoga, and acupuncture.\textsuperscript{51} For instance, multiple studies have shown that physical activity interventions can significantly reduce symptoms of depression, with aerobic exercise producing comparable effects to psychotherapy and antidepressants in cases of depression with mild to moderate symptoms.\textsuperscript{57-59} According to a meta-analysis study of 17 randomized control trials (RCTs) on massage therapy in people with depression, massage therapy was associated with significantly reduced depressive symptoms.\textsuperscript{60} Furthermore, acupuncture has long been used in Asian medicine, and while more trials are needed, it has the potential in reducing depression during pregnancy.\textsuperscript{61, 62} This intervention is carried out with the thought that the body is composed of a balance of energy, and acupuncture uses thin needles to stimulate anatomical points on the body in order to restore vital energy flow that has been blocked.\textsuperscript{51}

Auricular acupressure (AA) is similar to acupuncture and can be used to treat or improve a wide range of health conditions by stimulating acupoints on the ear corresponding to specific areas of the body.\textsuperscript{63} For this process, a seed or magnetic bead is typically secured at the acupoint of interest with adhesive tape and may require manual pressure for stimulation.\textsuperscript{64} Traditional Chinese medicine suggests effectiveness of AA through mediating the yin-yang balance of energy (qi) and blood flow.\textsuperscript{65} Another theory
proposes that AA can reduce symptoms of anxiety by decreasing adrenocorticotropic hormone concentrations and by regulating neurotransmitter concentrations like 5-hydroxytryptamine. A commonly used acupoint is called Shenmen, which can be found at the apex of the triangular fossa of either ear. This region is innervated by a branch of the vagus nerve and when stimulated, can produce parasympathetic nerve activity. Stimulation of the Shenmen acupoint can produce pain relief, relaxation, decreased postoperative nausea and vomiting, and calming effects.

AA has been studied in the treatment of anxiety and depression in many different populations. One study showed effectiveness of AA in reducing the need for sedatives and anti-anxiety medication in post-menopausal women with anxiety. Another study showed successful reduction in anxiety and pain in elderly patients before hip surgery. Similarly, a recent study showed improvement in anxiousness, depressed mood, and sleep quality in nursing students. Despite all these studies, there has not been a trial evaluating the effectiveness of magnetic bead AA on depression and anxiety in mothers with PPD. AA has the advantages of being cost-effective, non-invasive, and patient-acceptable. This can be a beneficial intervention and would help overcome barriers for mothers with PPD who may be seeking an alternative treatment to psychotherapy and/or medication. In Taiwan, this is considered an easy intervention to learn and can be performed by patients themselves or caregivers without costly visits. Advancements in the use of AA in other countries show the growth potential for AA use in the United States. AA is a potentially valuable intervention that can fall under the skill set of physician assistants to help treat or improve a wide range of conditions for their patients.
1.2 STATEMENT OF THE PROBLEM

Peripartum depression is a prevalent and serious mental health problem, with approximately 1 in 4 women experiencing depression following childbirth and only 1 in 10 receiving evidence-based treatment. Despite pharmacotherapy and psychotherapy as available treatments, barriers still stand in the way such as stigma, cost, time investment, transportation, and adverse effects on both mother and infant.

Pharmacotherapy includes multiple unwanted side effects such as dizziness and inattention, which contributes to poor patient compliance and effectiveness. This can deter mothers and especially breastfeeding mothers due to the fear of exposing their infant to the drug. Two recent systematic reviews have argued that there is still insufficient evidence from clinical trials to make a firm recommendation for the use of antidepressant medication for PPD. Furthermore, results have shown little evidence of superiority of medication over appropriate placebo controls. On the contrary, psychotherapy is recommended and has shown effectiveness in PPD, but treatment is limited by the lack of providers or the cost associated with accessing these services.

There is a clear need for alternative therapies that will be both effective and appealing to patients. Trials have begun to investigate complementary and alternative therapies for PPD in order to broaden treatment options and reach more women, one of which includes auriculotherapy. Magnetic bead auricular acupressure is a cost-effective, non-invasive, patient-acceptable intervention that has been shown to be effective in reducing anxiety and depressive symptoms in other population groups, however, has not been investigated yet in mothers with PPD.
1.3 GOALS AND OBJECTIVES

The goal of this novel, randomized control trial is to investigate whether magnetic bead auricular acupressure will decrease depression and anxiety severity in mothers with PPD. The primary aim of this study is to evaluate and compare the mean change in depression severity in mothers with PPD, assessed using the 17-Item Hamilton Depression Rating Scale (HAMD-17), between those using magnetic bead auricular acupressure and those using sham auricular acupressure. As a secondary measure of depression, the mean change in depression severity will also be assessed using the Edinburgh Postnatal Depression Scale (EPDS). Additionally, we will evaluate and compare the mean change in anxiety severity, assessed using the Generalized Anxiety Disorder 7-Item (GAD-7) questionnaire.

1.4 HYPOTHESIS

Mothers with peripartum depression (aged 18-45) using magnetic bead auricular acupressure will have a statistically significant mean difference in depression severity, assessed using the Hamilton Depression Rating Scale (HAMD-17), after 4 weeks, as compared to mothers using sham auricular acupressure.

1.5 DEFINITIONS

Hamilton Depression Rating Scale (HAMD-17): A 17-item questionnaire that is used to help identify and determine severity of depression.

1.6 REFERENCES


47. McDonagh MS, Matthews A, Phillipi C, et al. Depression drug treatment outcomes in pregnancy and the postpartum period: A systematic review and meta-


Chueh K, Chang C, Yeh M. Effects of Auricular Acupressure on Sleep Quality, Anxiety, and Depressed Mood in RN-BSN Students With Sleep Disturbance. 2018;doi:10.1097/JNR.0000000000000209


CHAPTER 2: REVIEW OF THE LITERATURE

2.1 INTRODUCTION

A review of the literature was conducted between December 2022 and April 2023 using Pubmed, Scopus, Ovid, and ScienceDirect. The medical subject heading terms used to search these databases included “postpartum depression”, “depression”, “depressive disorder”, “anxiety”, “acupressure”, and “auriculotherapy”. Additional search terms included perinatal depression, postnatal depression, auricular therapy, ear therapy, vagus nerve stimulation, magnetic bead, magnetic pellet, magnetotherapy, stress, and mental health. Clinical trials, meta-analyses, and systematic reviews were analyzed for pertinence to our study. Three articles published in other languages, two in Korean and one in Persian, were translated to English and included into the review based on their relevance and contribution to the advancement of the literature. Several articles were also extracted from the reference lists of other articles.

2.2 REVIEW OF EMPIRICAL STUDIES

2.2.1 Auriculotherapy

Auriculotherapy has been a longstanding form of therapy, originating from ancient Chinese medicine. This intervention includes modalities of auricular acupuncture and auricular acupressure, both of which produce effects through the stimulation of specific acupoints on the external ears that are thought to have different functions and/or target particular areas of the body.\textsuperscript{1,2} Auricular acupuncture utilizes needles which can be either temporary or semipermanent, and can even include an electrical component.
Auricular acupressure (AA) on the other hand, uses medicinal seeds or magnetic pellets on ear acupoints, creating effects with pressure stimulation and/or magnetotherapy.³

The World Health Organization (WHO) recognized AA as a treatment for diseases in 1990, and since then it has been systematically applied in various diseases.⁴ The literature review revealed beneficial effects of AA with small to large effect sizes on a number of outcomes including hypertension⁵, pain management⁶, myopia⁷, constipation⁸, postpartum lactation⁹, sleep disturbances³, anxiety¹⁰, and depression¹¹. Although AA has been explored in a breadth of disease states, there has yet to be a RCT exploring the effects of magnetic bead AA on PPD.

2.2.2 Auricular Acupressure on Depression

A review of the literature demonstrated a positive impact between AA and its effects on depression in several population groups. College students, and especially those concurrently working full-time, often undergo great amounts of stress. This can come with a string of adversities such as sleep disturbances, depression, and anxiety. In a one-group, quasi-experimental study by Chueh et al. (2018), students with sleep disturbances were recruited from a 2-year registered nurse to Bachelor of Science in nursing (RN-BSN) program in Taiwan; students underwent a 4-week AA intervention with magnetic pellets.³ Sleep quality, depressed mood, and anxiety scores were measured before and after intervention with the Pittsburgh Sleep Quality Index (PSQI), Beck Depression Inventory-II (BDI-II), and Beck Anxiety Inventory (BAI), respectively. Results from the study demonstrated significant decreases in all three tests from baseline to post-intervention (p < 0.001).³ Furthermore, sleep quality, anxiety, and depression improved by 26.7%, 43.5%, and 25% respectively.³ However, this study had several limitations
including the lack of a control group. Although these results provide preliminary support for AA, the absence of a sham or control arm limits the quality of evidence obtained from this study. The long-term effects of AA beyond the 4-week intervention period are also unknown since this was a short-term study; thus, a longitudinal study to determine the persistence of any treatment effect is required.

A recent study conducted by Tseng et al. (2021) also found a beneficial effect of AA on symptoms of depression in a cohort of older adults. Depression is not uncommon in older adults, affecting approximately 8-15% in communities, and up to 30-45% in those living in long-term care (LTC) institutions.\textsuperscript{12} Forty-seven older adults from Taiwan were recruited in a two-arm, single-blinded clinical trial to evaluate the effects of AA on depression and anxiety in elderly living in LTC institutions.\textsuperscript{11} Participants were randomized to either the experimental group with a magnetic bead or a control (sham) group with a blank patch. Depression scores were assessed using the Geriatric Depression Scale (GDS) – Short Form. Results after two weeks of AA demonstrated a statistically significant difference in both depression and anxiety between the two groups (both p < 0.05).\textsuperscript{11} The average GDS score in the experimental group decreased from 8.74 ± 2.31 (baseline) to 7.23 ± 2.64 (at 7 days of intervention) to 5.35 ± 2.08 (at 14 days of intervention). Meanwhile, the average GDS score in the control group trended upwards from 8.17 ± 3.08 (baseline) to 8.24 ± 3.16 (at 7 days of intervention) to 8.58 ± 3.53 (at 14 days of intervention).\textsuperscript{11} Limitations of this study included a small sample size, blinding of only the participants causing a possible detection bias, and unknown subsequent effects of AA beyond 14 days due to a short monitoring period.
Another recent RCT by Yin et al. (2022) investigated the effects of AA on depression in stroke patients.\textsuperscript{13} Fifty-six participants with post-stroke depression were randomly assigned to either the AA group or sham group, and change in symptoms of depression and quality of life were evaluated using the Hamilton Rating Scale for Depression (HAMD-17), Zung Self-Rating Depression Scale (SDS), and the World Health Organization Quality of Life Brief Version (WHOQOL-BREF) questionnaire. All outcomes demonstrated a statistically significant improvement after 4 weeks of intervention in both groups (p < 0.01), with even greater changes in the AA group than the sham group (p < 0.05).\textsuperscript{13} The mean change in HAMD-17 and SDS scores after 4 weeks demonstrated a large effect size of AA on depression (Cohen’s $d = 1.67$ and 0.93 respectively).\textsuperscript{13} Data from this trial suggests that AA could be effective in alleviating depression and improving quality of life in post-stroke depression patients, however, this conclusion needs to be verified with a well-designed large scale RCT with longer term follow-up.

Lastly, Kim et al. (2022) also found supporting evidence for AA in reducing depression in a population of nurses in Korea.\textsuperscript{14} A two-arm, RCT study was conducted, investigating changes in depression using the Patient Health Questionnaire (PHQ-9). After two weeks of either the AA intervention (pressure stickers with aluminum or copper projections) or sham AA, a significantly greater mean difference in PHQ-9 scores after AA in the experimental group (-4.11 ± 2.27) was observed, as compared to the control group (-1.72 ± 3.82) ($t = 2.28$, $p = 0.03$).\textsuperscript{14} However, as this study had a sample size of 40, future studies with a larger number of participants are recommended.
2.2.3 Auricular Acupressure on Anxiety

Since we will also be studying AA and its effects on anxiety as a secondary aim, we reviewed the literature for the effects of AA on anxiety in different population groups. Of the numerous studies found, there were overlap with a few of the previously mentioned studies that discussed alleviation of depressive symptoms. From Chueh et al. (2018), anxiety symptoms in RN-BSN students were improved by 43.5% after 4 weeks of AA intervention ($p < 0.001$).3 Tseng et al. (2021) found that when investigating the effects of AA on anxiety in elderly patients in LTC institutions, there was no significant difference in anxiety scores between the experimental and control group at 7 days (Cohen’s $d = 0.18$), but there was a significant difference after 14 days of intervention representing a medium effect size (Cohen’s $d = 0.55$; $p = < 0.05$).11

Kuo et al. (2016) also found a beneficial effect of AA on symptoms of anxiety in a single-blinded, RCT investigating AA therapy on anxiety and fatigue in women who underwent caesarean sections in Taiwan.15 AA was applied to the Shenmen acupoint for three minutes, twice a day, from day 1 to day 4 postpartum. Anxiety symptoms were measured using the 20-item self-report State Anxiety subscale of the State-Trait Anxiety Inventory (STAI). Those in the vaccaria seed acupressure group had significantly lower mean anxiety symptoms than women in the control group at 5 days postpartum (mean difference = 3.8, $p < 0.01$).15 The Cohen’s $d$ score of 0.81 demonstrates a large effect size of AA therapy on anxiety in this population group. These results are consistent with prior studies showing evidence of AA reducing anxiety symptoms in women undergoing in-vitro fertilization16 and in women going through peri- or early menopause17.
Given the high levels of stress in healthcare, Olshan-Perlmutter et al. (2019) investigated magnetic pellet AA on anxiety and burnout in behavioral healthcare providers in North Carolina. Anxiety severity was measured using the General Anxiety Disorder questionnaire (GAD-7). After 6 weeks, there was a statistically significant improvement in the AA treatment group with a mean total GAD-7 score from 6.14 to 3.65 (t = 4.6; p < 0.01), while no improvement was noted for the waitlist (control) group with a score from 5.91 to 5.65 (t = 0.38; NS). Furthermore, the waitlist group began the true AA intervention at week 7 and a significant decrease in GAD-7 scores was noted after 6 weeks (5.91 to 4.00; t = 3.2; p <0.05). Recommendations for future studies include a longer follow-up period and investigation of a dose response as it is not known whether one needs to have continuous treatment or if maintaining the pellet for one or two days would have produced the same response.

A systematic review and meta-analysis were conducted by Au et al. (2015) on the effects of acupressure on anxiety prior to surgery or treatment for isolated hip fractures, abdominal illnesses, renal-related illnesses, cardiac dysrhythmias, and adults undergoing elective surgeries. Interventions took place in either a hospital setting before the scheduled treatment or on the way to the hospital in an emergent setting. The results showed that all five RCTs had a greater overall reduction in anxiety in the acupressure group than in the sham controls (standardized mean differences = -1.11; 95% CI -1.61 to -0.61; p < 0.0001). A closer look at these trials illustrated risks for potential bias. Regarding the randomization process to prevent selection bias, although they were all described as ‘randomized’, only five of the seven trials reported detailed randomization methods. As for allocation concealment, only three trials described the process, leaving
questionable selection bias in the other trials. However, it was noted that all studies employed a sham control to blind participants to the allocated intervention, controlling for performance bias. Given that some of these trials applied AA at two different acupoints while others applied AA to only one, further studies are recommended to reach a firm conclusion about the optimal number of points required for effect. Moreover, there are only a few trials evaluating the effect of AA on anxiety among adults and thus, more rigorous, well-designed research following guidelines is warranted to strengthen these results.

### 2.2.4 Auriculotherapy on Peripartum Depression

Our literature review resulted in two articles that investigated auriculotherapy, however, not magnetotherapy, on mothers with PPD. A clinical trial by Ghaemmaghami et al. (2021) evaluated the effect of AA, using an electric pointer device, on PPD in nulliparous women in labor. Auriculotherapy was deployed at 3 different instances: 4-6cm dilated, 6-8cm dilated, and 6 hours after delivery. Stimulation was applied between contractions for 30 seconds in both ears at intervals of 10 minutes and then again in the postpartum period. They found no significant difference in maternal depression (assessed by the Beck questionnaire) between the experimental and control group, with a p-value of 0.549, where p < 0.05 is considered statistically significant. The authors emphasized that the short treatment period including only a few auriculotherapy sessions could explain the absence of a treatment effect on depression reduction between the two groups, thus recommending that future studies should apply the intervention for a longer period.

In contrast, a study by Kim et al. (2019) found a reduction in the severity of PPD and fatigue in early postpartum mothers with the use of AA. The authors conducted a
nursing intervention, which included an educational session on PPD; ear massage using finger pressure; stimulation from pressure rings which were pressed 4 times a day, every 3 days, and removed after 2 days; and emotional support. Depression symptoms were measured with the Korean version of the Edinburgh Postnatal Depression Scale (EPDS). The experimental group showed a mean EPDS score decrease of 1.30 ± 2.49 points after intervention (z = -2.15, p = 0.032) while no significant change was observed in the control group: 0.20 ± 2.19 point increase (z = -0.74; p = 0.462). The frequency of application was higher than in the previously mentioned study by Ghaemmaghami et al. (2021); however, this intervention program also included additional components such as an educational and emotional support session which could have contributed to the reduction in depression severity. Future studies can benefit from recruiting a larger sample size and establishing a longer follow-up period.

2.3 REVIEW OF STUDIES TO IDENTIFY CONFOUNDING VARIABLES

There are multiple potential confounding variables within the procedure for AA. The first example is the various types of auriculotherapy that can be administered. Studies have used a wide range of interventions such as magnetic beads/pellets, plastic beads, medicinal seeds, semi-permanent needles (ASP), and steel needles. One study by Kurebayashi et al. (2017) compared AA using seeds versus semi-permanent needles for reducing anxiety in nursing professionals and found better results for semi-permanent needles, however, cautioned that this modality can lead to local pain and infection.

Other confounding factors for AA include the frequency of application, duration of intervention, strength of stimulation, and selection of acupoints. Each acupoint holds a
particular function and/or corresponds to a particular area of the body; while the Shenmen point is used most frequently for depression and anxiety, different acupoints or combinations of acupoints can be stimulated for effect. For instance, in a meta-analysis by Vieira et al. (2022) which included nine studies evaluating the effects of AA on anxiety disorders, the most frequently used acupoint was Shenmen or Cosmonaut, followed by Hypophysis, Hippocampus, and Sympathetic Master Point. In a study investigating AA on depression in post-stroke patients by Yin et al. (2022), five auricular points (Shenmen, Sympathetic, Heart, Liver, and Subcortex) were used. In contrast, a study by Tseng et al. (2021) evaluating the effects of AA on depression in long-term care residents used only the one Shenmen point. Nonetheless, both studies concluded effectiveness of AA in alleviating depressive symptoms in their population groups.

Additionally, numerous confounding variables for PPD have not been consistently considered in trials of AA. For example, age, sex of the baby, multiparity, gestational diabetes, cesarean section, previous stressful life event, history of depression, social support and relationships, self-esteem, and birth/infant related factors (multiple births, preterm or low-birthweight infants, negative birth experience) may all contribute to PPD. One meta-analysis showed a 43% increased risk for PPD from intimate partner violence, and another meta-analysis similarly found a 3-fold increase in the probability of high levels of depressive symptoms in the postpartum period with partner violence during pregnancy. Studies have shown that cesarean sections have been associated with PPD, with highest risk in women undergoing emergency sections. It is thought that the increased patient stress related to surgery may increase risk of PPD which also explains the higher probability of PPD after emergency cesarean sections.
to a meta-analysis by Beck (2001) on the basis of 11 studies, a history of depression including prenatal depression or maternity blues, has a medium effect size on the likelihood of developing PPD.\(^{44}\) This conclusion was supported by Robertson et al. (2004) with a study of over 14,000 participants confirming that the strongest predictors of PPD were depression during pregnancy and a previous history of depression.\(^{45}\)

Another confounding variable found frequently in the literature review was a lack of social support. A study by Chen et al. (2019) found the lack of social support as a cause of PPD among immigrant mothers\(^{46}\); a systematic review supported this conclusion, stating that in African American and Hispanic women, the lack of social support may increase the prevalence of PPD in this group.\(^{47}\) Moreover, two studies found that increased social support could significantly reduce the risk of PPD.\(^{48, 49}\) In regard to age, Zaidi et al. (2017) noted that being a young female (younger than 25 years old) was a risk factor for PPD (\(p = 0.040\)), which could be associated with the stress of early marriage and childbirth responsibility.\(^{35}\) A study evaluating risk factors for postnatal depression in Chinese women supported this statement, showing a significant association between younger age and PPD.\(^{50}\) Zeidi et al. (2017) stated that multiparous postnatal women are also at increased risk for PPD, which could be due to the increased level of maternal stress in terms of responsibility for their other children.\(^{35}\) Finally, the likelihood of developing PPD is higher among mothers who face societal pressure, particularly in certain developing countries, to give birth to a male child. Consequently, giving birth to a female may contribute to PPD in these regions.\(^{51, 52}\)
2.4 REVIEW OF RELEVANT METHODOLOGY

2.4.1 Study Design and Setting

Several RCTs have been conducted to examine the effects of AA on psychiatric conditions in a variety of patient populations; some were not RCTs, such as a one-group, quasi-experimental study, however, most designs were RCTs which utilized a two-arm design to compare AA versus a control. A RCT comparing an experimental group against a control group offers the highest quality evidence regarding the effect of the independent variable on the dependent variable.

Our proposed study will be a multicenter, single-blinded, two-arm, randomized control trial to investigate the benefits of magnetic bead AA compared to sham acupressure in new mothers (aged 18-45) with peripartum depression. The study centers included in this study will be hospitals that are part of the greater Yale New Haven Health System: Yale New Haven Hospital, Bridgeport Hospital, Greenwich Hospital, Lawrence and Memorial Hospital, Westerly Hospital, and the Northeast Medical Group. This system includes a diverse selection of centers that comprises the largest healthcare system in Connecticut and allows for a larger sample of women with varying demographics. Participants will be recruited using convenience sampling and will be randomly allocated to an intervention or control group on a 1:1 basis.

2.4.2 Selection Criteria

Available literature on the treatment of PPD was examined to determine the inclusion and exclusion criteria for our proposed study. Commonly found requirements for participation in studies included: mothers aged 18-45, primiparous women, vaginal delivery, delivery within 6 months, delivery of a healthy infant (at least 36 weeks gestation).
weeks gestation\textsuperscript{56}, and a PHQ-9 score of $\geq 10$ (predictive of Major Depressive Disorder)\textsuperscript{54}. As discussed earlier, infant related factors such as preterm or low-birthweight is a potential confounding variable, thus, setting a criteria for the delivery of a healthy infant will help control for these factors. Similarly, an inclusion criterion for vaginal deliveries will control for cesarean sections playing a role in PPD. The PHQ-9 is a commonly used and effective screening tool to detect for the presence and severity of depression.\textsuperscript{54} This 9-item questionnaire is a highly sensitive (73\%-88\%) and highly specific (88\%-98\%) depression scale\textsuperscript{54} that has been used in past studies for women with PPD\textsuperscript{54, 56, 57} and will be used in our proposed study as well.

The exclusion criteria for our proposed study are also consistent with prior studies on treatment for PPD and/or the AA intervention. Participants will be excluded from our study if they meet the following: trauma or inflammation of either pinna\textsuperscript{11, 13, 28}; suicidal ideation\textsuperscript{56, 57}; thoughts of harming their baby\textsuperscript{56}; current or past diagnosis of bipolar disorder, schizophrenia, or other psychotic disorder\textsuperscript{54-56}; current psychotic symptoms\textsuperscript{56}; substance use disorder\textsuperscript{57}; current illegal drug use (based on self-report or positive urine screen)\textsuperscript{56}; current use of antidepressants, anxiolytics, antipsychotics, acupuncture/acupressure, or other complementary and alternative medicine\textsuperscript{28, 54, 56, 57}; ongoing treatment with psychotherapy\textsuperscript{54, 56, 57}; current participation in another clinical trial for PPD. Exclusion of variables such as use of psychiatric medication or other complementary and alternative medicine therapies that may reduce depression and/or anxiety symptoms will help ensure that the difference in our results are due to the intervention. For participant safety, individuals in dangerous situations, such as mothers experiencing suicidal ideations and/or thoughts of harming their baby, will be excluded.
from the study and emergency mental health intervention will be required.\textsuperscript{57, 58} Additionally, ensuring that AA is being applied to ears clear of trauma and/or inflammation will prevent any further irritation or damage to the area and allow the application of AA without complications.

2.4.3 Intervention and Control Group

Our proposed study will be using magnetic bead AA as the intervention for several reasons. First, auricular acupuncture utilizes needles as the source of stimulation, which may not be widely accepted by all participants.\textsuperscript{53} In addition to a fear of needles, participants are at risk for inflammation or infection of the site, and blood-borne diseases if strict aseptic techniques are not followed.\textsuperscript{53} Second, while seed acupressure has also been used in past studies, this treatment approach requires participants to remember to apply pressure to the site multiple times a day. We decided not to use this modality since new mothers with PPD may have sleep disturbances and an increased cognitive load, which can cause missed acupressure sessions and bias our results.\textsuperscript{53, 58} Magnetotherapy is ideal for this patient population since it is non-invasive, less traumatic, and convenient as it does not require pressing.\textsuperscript{53} Although the exact biomechanics of how magnets affect the human body has not been determined, it is theorized that blood acts as a possible conductor of magnetic energy flow, and consequently increases the delivery of oxygen and nutrients to tissues.\textsuperscript{59} Research on magnetotherapy is limited and controversial, thus the therapeutic effect of using magnetic bead as an auricular therapy for treating PPD merits further study.

The strength of magnetization will be consistent with a prior study, by Olshan-Perlmutter et al. (2019), which found beneficial effects of AA on anxiety and burnout in
We will be using 800 gauss low magnetic intensity Ferrite ear beads, which have had no documentation of being associated with significant injury. The Shenmen acupoint was selected for our study since it is one of the classical National Acupuncture Detoxification Association auricular acupoints and has been used widely in many studies for treatment of depression and anxiety. Activation of the auricular Shenmen point helps with the maintenance of qi and blood, release of heat, clearance of phlegm, alleviation of stress, calming, psychological adjustment, and regulation of blood pressure. The magnetic bead will be secured to the acupoint with hypoallergenic tape each week for a total intervention duration of 4 weeks. These parameters are consistent from a study by Tseng et al. (2021) and is supported by previous studies which performed acupressure interventions for intervals ranging from 2-6 weeks.

We decided the control group will receive a seed that will be taped and secured to an acupoint irrelevant to producing effects on depression and anxiety. From our literature review, studies have set their control group either as a waitlist group, usual care group, or a group that was given a blank patch. Although utilization of a blank patch seemed reasonable and initially favorable, we decided against this approach as it may be possible for participants to tell whether or not there is a bead underneath the taped area, thus leading to an unblinding of participants. After a further search in the literature, we found studies that applied AA to different auricular acupoints which were not predicted to produce an effect on the condition being studied. Yin et al. (2022) chose acupoints unrelated to depression in stroke patients: Knee, Lumbosacral Vertebrae, Shoulder, and Eye. We chose the knee acupoint since it is unrelated to depression and anxiety in our population for PPD. Finally, the control group for our study will utilize a seed rather than
a magnetic bead to avoid potentially producing a magnetic field and altering results since the Knee acupoint is proximal to the Shenmen point.

**2.4.4 Primary and Secondary Outcome Measures**

The primary outcome measure for our study will be the mean change in depression severity, assessed using the Hamilton Depression Rating Scale (HAMD-17). We chose the HAMD-17 scale for our study because it has become the standard for clinical trials and is among the most widely used scale for controlled clinical trials in depression. It is also sensitive to treatment change and is a valid indicator of depression severity in PPD. The questionnaire takes approximately 12 minutes to complete and the total score is calculated by summing the score of each item, for a total score of 0 to 54. The generally accepted cut-off scores for each category are: 0-6 for no indication of depression, 7-17 for mild depression, 18-24 for moderate depression, and over 24 for severe depression. In order to quantify the effects of AA, the HAMD-17 questionnaire will be administered at baseline (T0), then two weeks (T1), four weeks (T2), three months (T3), and six months (T4) after the start of treatment. We will subsequently use these scores to calculate the net change from baseline at each time point.

The mean change in Edinburgh Postnatal Depression Scale (EPDS) scores will also be calculated as a secondary measure of depression. The 10-item EPDS, with a sensitivity of 86% and specificity of 78%, is a commonly utilized questionnaire that can be self-administered and typically completed within 5 minutes. The questions reflect on the past 7 days and are scored up to 30 points, with 10 or greater indicating possible depression. Similarly, the EPDS will be administered at T0, T1, T2, T3, and T4, then the net change from baseline at each time point will be calculated.
Moreover, we will calculate the mean change in anxiety symptoms using the General Anxiety Disorder 7-Item (GAD-7) questionnaire. As mentioned previously, depression and anxiety frequently occur together so it is important that we monitor anxiety symptoms over the course of the study. The GAD-7 contains 7 questions asking about core anxiety symptoms in the previous two weeks, for a sum score ranging from 0 to 21, with higher scores indicating worse anxiety.\textsuperscript{64, 65} This questionnaire has been validated in postpartum samples\textsuperscript{66, 67} and has been used in PPD RCTs such as one by Van Lieshout et al. (2021).\textsuperscript{65} Like the process for administering the EPDS, the GAD-7 questionnaire will be filled out by patients at T0, T1, T2, T3, and T4, then the net change from baseline at each of these time points will be calculated.

2.4.5 Sample Size and Statistical Significance

The literature review did not yield any RCTs examining the effect of magnetic bead AA on mothers with PPD. Therefore, our sample size calculation includes data from two studies. We calculated the relative effect in these studies and extrapolated this information to estimate the effect size for our intervention and study population.

To determine the relative effect of AA, a study by Liu et al. (2021)\textsuperscript{68}, investigating the effects of acupuncture on anxiety and depression in patients with chronic insomnia, was used under the assumption that electroacupuncture would produce similar results to acupressure. After 4 weeks of acupuncture, the mean change in HAMD-17 score was found to be $-4.96 \pm 2.14$.\textsuperscript{68} The mean of the population was extrapolated from a study by O’Hara et al. (2000) who evaluated the efficacy of interpersonal psychotherapy on PPD.\textsuperscript{69} They found that the waitlist (control) group in this study had a mean change in HAMD-17 score of $-1.5 \pm 5.25$ after 4 weeks. Using the relative effect of
auriculotherapy on patients with chronic insomnia and the relative effect of a waitlist period for PPD, we obtained an estimation of the effect that acupressure would have on PPD. Drawing on these summary statistics, we calculated Cohen’s $d = 0.87$ representing a large effect size for the association between AA and PPD symptoms. A predicted 6.66% attrition rate, as noted in the study by Liu et al. (2021)\textsuperscript{68}, was also taken into consideration in determining the final sample size. We will use a two-sided test with $\alpha = 0.01$ and power of 80%. Details on the sample size calculation can be found in Chapter 3 and Appendix A.

2.5 CONCLUSION

The literature review supports the need for further investigation of complementary and alternative medicine for PPD. The use of AA has been widely explored in a variety of conditions, but the literature highlights the need for a RCT investigating the effect of magnetic bead AA for treatment of PPD. A single-blinded, sham controlled, randomized trial will most effectively examine the proposed benefit of magnetic bead AA on mild to moderate severity PPD. This study aims to fill this gap in the literature and potentially help expand treatment options for mothers with PPD.

2.6 REFERENCES

3. Chueh K, Chang C, Yeh M. Effects of Auricular Acupressure on Sleep Quality, Anxiety, and Depressed Mood in RN-BSN Students With Sleep Disturbance. 2018;doi:10.1097/JNR.0000000000000209


CHAPTER 3: STUDY METHODS

3.1 STUDY DESIGN

We propose a two-arm, single-blinded, randomized controlled trial to investigate the effects of magnetic bead auricular acupressure compared to sham acupressure in new mothers (aged 18-45) with peripartum depression. Participants will be assigned to either Group 1, the intervention group, or Group 2, the control group, by a computer-generated randomization. Both groups will receive their allocated intervention for a total of 4 weeks by a licensed acupuncturist. The Hamilton Depression Rating Scale (HAMD-17), Edinburgh Postnatal Depression Scale (EPDS), and General Anxiety Disorder (GAD-7) will be administered at the following time points: baseline (pre-intervention), then at 2 weeks, 4 weeks, 3 months, and 6 months after the start of treatment.

3.2 STUDY POPULATION AND SAMPLING

The study population will include new mothers (aged 18-45) with mild to moderate severity peripartum depression who have given birth in the Yale New Haven Health System. Eligible patients will be recruited using convenience sampling from the Yale New Haven Health System hospitals for 6 months. The provider caring for the patient will administer a Patient Health Questionnaire (PHQ-9) within 3 days after delivery (score of ≥ 10 is predictive of Major Depressive Disorder). Eligible patients who meet inclusion criteria (see Table 1) will be invited to participate in a Structured Clinical Interview for a DSM-V (SCID) for diagnosis of Major Depressive Disorder with peripartum onset, and a HAMD-17 assessment video interview with a psychiatrist (see Appendix B for diagnostic criteria). Those with a HAMD-17 score of 7-24 (indicating mild to moderate depression) and who do not meet exclusion criteria based on the
presence of other psychiatric disorders (e.g., bipolar disorder), will be asked to participate in an in-home visit to review study protocol and consent to be randomized. After consenting, participants will receive a demographic survey, GAD-7, and EPDS assessment to be filled out electronically using Qualtrics.

Table 1: Study Eligibility

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
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<tbody>
<tr>
<td>• Mothers aged 18-45</td>
<td>• Trauma or inflammation of either pinna</td>
</tr>
<tr>
<td>• Primiparous women</td>
<td>• Suicidal ideation</td>
</tr>
<tr>
<td>• Vaginal delivery within 6 months</td>
<td>• Thoughts of harming their baby</td>
</tr>
<tr>
<td>• Delivery of a healthy infant (at least 36 weeks gestation)</td>
<td>• Current or past diagnosis of bipolar disorder, schizophrenia, or other psychotic disorder</td>
</tr>
<tr>
<td>• PHQ-9 score of ≥ 10 (predictive of Major Depressive Disorder)</td>
<td>• Current psychotic symptoms</td>
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<tr>
<td></td>
<td>• Substance use disorder</td>
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<tr>
<td></td>
<td>• Current illegal drug use (based on self-report or positive urine screen)</td>
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<tr>
<td></td>
<td>• Current use of antidepressants, anxiolytics, antipsychotics, acupuncture/acupressure, or other complementary and alternative medicine</td>
</tr>
<tr>
<td></td>
<td>• Ongoing treatment with psychotherapy</td>
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<tr>
<td></td>
<td>• Current participation in another clinical trial for PPD</td>
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</tbody>
</table>

3.3 SUBJECT PROTECTION AND CONFIDENTIALITY

We will obtain Yale Institutional Review Board (IRB) approval for our study prior to recruitment. The consent form for our study will outline the purpose of research, proposed study procedures, expected duration of study, potential risks and benefits, and confidentiality details. It will state that participation is voluntary and that participants have the right to decline participation at any point in time. A sample consent form is provided in Appendix C. Once consent is obtained, participants will be sent the demographic survey, GAD-7, and EPDS assessment to be completed electronically. To
ensure confidentiality, all electronically submitted forms will be accessed through university-approved, encrypted, and secured devices. All protected health information not in electronic form will be stored within a locked file cabinet, to which only direct research staff will have access. Additionally, all study personnel will be required to complete a Health Insurance Portability and Accountability Act (HIPPA) and Yale Human Subjects Protection training prior to the start of the study. Upon completion of the study, all collected information will be disposed of in a secure manner.

3.4 RECRUITMENT

Recruitment will primarily take place at the Yale New Haven Hospital System centers: Yale New Haven Hospital, Bridgeport Hospital, Greenwich Hospital, Lawrence and Memorial Hospital, Westerly Hospital, and the Northeast Medical Group. Patients aged 18-45 who delivered in these hospital sites will be provided with information about the study if they meet the selection criteria. Upon confirmation of mild to moderate severity PPD using the SCID-V and HAMD-17 questionnaire, the study team will schedule a time to meet with the participants who are interested in the study for an in-home visit to review study protocol and obtain consent for participation/randomization.

3.5 STUDY VARIABLES AND MEASURES

3.5.1 Independent Variables

The intervention will consist of magnetic bead auricular acupressure at the Shenmen acupoint. At each session, a licensed acupuncturist will visit the patient’s home, disinfect the external ear with 75% ethanol, identify the Shenmen acupoint of the ear with an electronic acupoint detection pen, and secure the bead in place with a hypoallergenic adhesive patch (see figure 1\(^1\)). After 7 days, the acupuncturist will return for the patient’s
next session where they will have the previously secured bead removed and a new bead placed on the other ear. There will be a total of 4 sessions for an intervention duration of 4 weeks. Beads will alternate between ears each session. If the bead falls off during the week, the acupuncturist will need return and place a new one as soon as possible.

![Figure 1: Auriculotherapy Beads with Adhesive Patches](image)

The sham (control) group will receive a vaccaria seed, which is similar in size to the magnetic bead, secured to the Knee acupoint with the same process as described in the intervention group. All other procedural aspects will be consistent with the intervention group for the remaining of the study. Importantly, all participants will be asked not to apply pressure to the site. See figure 2 below for the Shenmen and Knee acupoints.²
3.5.2 Dependent Variables

The primary outcome in our study will be the mean change in depression severity, assessed using the HAMD-17 questionnaire, from baseline (T0) to 4 weeks or the end of treatment (T2). Secondary outcomes will include the mean change in depression severity, using the HAMD-17 questionnaire, from baseline (T0) to 2 weeks (T1), 3 months (T3), and 6 months (T4). We will also measure the mean change in depression severity using the EPDS questionnaire, from T0 to T1, T2, T3, and T4. Lastly, we will measure the mean change in anxiety symptoms, assessed using GAD-7, from T0 to T1, T2, T3, and T4.

3.5.3 Potential Confounding and Explanatory Variables

PPD can be influenced by many variables which can subsequently impact study results. We will assess to ensure that factors such as age, race or ethnicity, body mass index (BMI), education level, occupation, marital status, and household income are balanced at baseline. Should the groups show differences on key demographic variables, we will collect data on additional potential confounding variables. HAMD-17, EPDS, and GAD-7 scores will also be assessed and compared between groups at baseline. We will analyze and compare categorical variables using chi-square and continuous variables.
using the Student’s *t*-test. Statistically significant differences in baseline characteristics found between study groups will be controlled for using the multivariate linear regression analysis. Please refer to Table 2 below for description and analysis of the baseline characteristics.

**Table 2: Baseline Characteristics Description and Analysis**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Magnetic Bead AA</th>
<th>Sham AA</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>mean ± SD</td>
<td>mean ± SD</td>
<td>Student’s <em>t</em>-test</td>
</tr>
<tr>
<td><strong>Race or Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>n (%)</td>
<td>n (%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td>Black/African American</td>
<td>n (%)</td>
<td>n (%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td>Asian</td>
<td>n (%)</td>
<td>n (%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
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<td>n (%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td>Other</td>
<td>n (%)</td>
<td>n (%)</td>
<td>Chi-square</td>
</tr>
<tr>
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<td></td>
<td></td>
</tr>
<tr>
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<td>n (%)</td>
<td>n (%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td>Normal</td>
<td>n (%)</td>
<td>n (%)</td>
<td>Chi-square</td>
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<tr>
<td>Overweight</td>
<td>n (%)</td>
<td>n (%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td>Obese</td>
<td>n (%)</td>
<td>n (%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td><strong>Education</strong></td>
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<td></td>
</tr>
<tr>
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<td>n (%)</td>
<td>Chi-square</td>
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<td>Chi-square</td>
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<td>Chi-square</td>
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</tr>
<tr>
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<td>n (%)</td>
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<td><strong>Occupation</strong></td>
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<td></td>
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<tr>
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<td>n (%)</td>
<td>Chi-square</td>
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<tr>
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<td><strong>Marital Status</strong></td>
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<td>Single</td>
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<td>Chi-square</td>
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<tr>
<td>Married</td>
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<td>Chi-square</td>
</tr>
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<td>Chi-square</td>
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</tr>
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<td>n (%)</td>
<td>Chi-square</td>
</tr>
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<td>n (%)</td>
<td>Chi-square</td>
</tr>
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<td>$40,001-60,000</td>
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<td>n (%)</td>
<td>Chi-square</td>
</tr>
<tr>
<td>Income</td>
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<td>n (%)</td>
<td>Chi-square</td>
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<tr>
<td>--------------</td>
<td>-----------</td>
<td>-----------</td>
<td>------------</td>
</tr>
<tr>
<td>$60,001-80,000</td>
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<td>$80,001-100,000</td>
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<td></td>
</tr>
<tr>
<td>&gt; $100,000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refused/Missing</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Baseline HAMD-17 score</th>
<th>mean ± SD</th>
<th>mean ± SD</th>
<th>Student’s t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline EPDS score</td>
<td>mean ± SD</td>
<td>mean ± SD</td>
<td>Student’s t-test</td>
</tr>
<tr>
<td>Baseline GAD-7 score</td>
<td>mean ± SD</td>
<td>mean ± SD</td>
<td>Student’s t-test</td>
</tr>
</tbody>
</table>

3.6 METHODOLOGY CONSIDERATIONS

3.6.1 Blinding

Participants will be blinded to the intervention; however, due to the nature of the intervention, the acupuncturist who will be administering either the true or sham acupressure will not be blinded. The rest of the team including the investigators; research assistant, who will be trained to collect data; and data analyst, will be blinded to the participants’ group allocation.

3.6.2 Assignment of Intervention

Participants will be randomly allocated at a 1:1 ratio using a computerized random number generator: (1) in the auricular acupressure group, subjects will receive hypoallergenic adhesive ear patches with magnetic beads (800 gauss) on the Shenmen acupoint starting on the left ear then alternating sides each week or (2) in the sham acupressure group, methods are identical to the auricular acupressure group, but hypoallergenic adhesive ear patches will contain a vaccaria seed on the Knee acupoint. One member of the research team will perform the randomization and allocation concealment using opaque, sealed envelopes. The individual will not be involved in the rest of the study.
3.6.3 Adherence

Adherence to study intervention will be assessed during mid-week telephone check-ins made by a research assistant. The assistant will be blinded to the intervention allocation and will call the participant to ensure the adhesive patch is still attached and no pressure has been applied to the site. In the event that the patch falls off or is removed prematurely, the acupuncturist will return to the patient’s home to have it replaced as soon as possible.

3.6.4 Monitoring of Adverse Events

Although adverse events are unlikely and not anticipated, the research assistant will ask during the mid-week telephone check-in about skin damage, infection, and allergic reaction to the ear. During weekly sessions, acupuncturists will also ask about adverse events and examine the acupoint areas after removing the previous bead/seed and prior to placing the next one. Any adverse event will be documented, and the study team will provide the participant with appropriate treatment and follow-up.

3.7 DATA COLLECTION

The HAMD-17 questionnaire will be administered by the psychiatrist, via an online video interview, at baseline and will continue to be administered at 2 weeks, 4 weeks, 3 months, and 6 months after the start of treatment (see Appendix D for questionnaire). Once consent has been received, each participant will complete an online, self-administered demographic survey, GAD-7, and EPDS assessment (see Appendix E-G). The research assistant will remind participants to complete the survey during the mid-week telephone check-in if it has not already been completed.
3.8 SAMPLE SIZE CALCULATIONS

The literature review did not yield any randomized controlled trials examining the effect of magnetic bead auricular acupressure on mothers with peripartum depression. Therefore, our sample size calculation is based on data from the two studies mentioned in chapter 2 with the primary outcome of mean change on HAMD-17 scores. The calculation was made with the Power and Precision (version 4) and G*Power software, and based on the assumption that a continuous, normally distributed outcome would be compared between the magnetic bead auricular acupressure group and sham acupressure group using a Student’s *t*-test. We calculated relative effect in the following studies and extrapolated this information to estimate the effect size for our intervention and study population.

The mean of the population was extrapolated from the study by O’Hara et al. (2000), using the mean change in HAMD-17 score of -1.5 ± 5.25 (19.8 ± 5.3 to 18.3 ± 5.2) in the waitlist control group, after 4 weeks. The relative effect of acupressure was calculated from the study by Liu et al. (2021), who found the mean change in HAMD-17 score of -4.96 ± 2.14 (12.79 ± 2.54 to 7.83 ± 1.65) after 4 weeks of acupuncture.

Using these values, a two-sided test with *α* = 0.01, and power of 80%, Cohen’s *d* was calculated to be 0.87, demonstrating a large effect size. Taking these numbers into consideration, we will recruit 33 patients per group. To account for a predicted 6.66% attrition rate, as noted in the study by Liu et al. (2021), 2 additional patients will be recruited to each group. With these additional participants, the final sample needed for our study is 70 patients with 35 in each group. A summary of the sample size calculation is provided in Appendix A.
3.9 ANALYSIS

Descriptive statistics will be used to describe and compare groups at baseline. As mentioned previously, categorical variables (race or ethnicity, BMI, education, occupation, marital status, household income) will be analyzed using the chi-square test and continuous variables (age, HAMD-17 score, EPDS score, GAD-7 score) will be analyzed using the Student’s t-test.

Statistical analyses will be carried out using the intention-to-treat principle. The primary outcome, mean change in HAMD-17 score from baseline to post-intervention, will be compared between groups using a Student’s t-test. The mean change in HAMD-17 score from baseline to the rest of the time points (2 weeks, 3 months, 6 months) will be compared between groups using analysis of variance (ANOVA) with repeated measures. The mean change in EPDS and GAD-7 scores from baseline to 2 weeks, 4 weeks, 3 months, and 6 months, will also be compared between groups using ANOVA with repeated measures. For all procedures, the statistical tests will be two-tailed with $\alpha = 0.01$.

3.10 TIMELINE AND RESOURCES

Once the study application is submitted and IRB approval is obtained, recruitment in the Yale New Haven Hospital System centers will commence. Site recruitment will be ongoing for 6 months or until the enrollment goal has been achieved. During the recruitment period, those who meet eligibility criteria and have mild to moderate depression, will be invited to the study. Once screening/enrollment is completed and consent is obtained, participants will be randomized to either the intervention group with magnetic bead auricular acupressure or the sham (control) group for 4 weeks.
Assessments and follow-ups will occur at baseline, 2 weeks, 4 weeks, 3 months, and 6 months. The entire study is expected to finish in under two years. See Figure 3 below for a diagram of the proposed study timeline.

The personnel requirement for the study will be a principal investigator and co-investigator for overseeing the study progress, and providers such as physicians, nurse practitioners, and physician assistants who will recruit patients at the study sites. Three licensed acupuncturists are needed for administration of AA and a psychiatrist will be needed for interval assessments. Two research assistants will be needed: one for data entry and mid-week telephone check-ins, and another for the randomization and allocation process. Additionally, a data analyst will be needed.
Figure 3: Study Design

Enrollment: 6 months
Baseline survey +
HAMD-17, EPDS, and GAD-7 assessments

Allocation

Magnetic Bead Auricular Acupressure

Sham Auricular Acupressure

Week 1: AA is applied on the left ear

Week 2: AA is removed from the left ear and applied on the right ear +
HAMD-17, EPDS, and GAD-7 assessments at the end of the week

Week 3: AA is removed from the right ear and applied on the left ear

Week 4: AA is removed from the left ear and applied on the right ear +
HAMD-17, EPDS, and GAD-7 assessments at the end of the week +
Intervention is completed and removed at the end of the week

3 Months: HAMD-17, EPDS, and GAD-7 follow-up assessments

6 Months: HAMD-17, EPDS, and GAD-7 follow-up assessments

3.11 REFERENCES


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CHAPTER 4: CONCLUSIONS

4.1 ADVANTAGES AND DISADVANTAGES

Auriculotherapy has been studied in a breadth of conditions and population groups, however, few studies have examined the impact of auriculotherapy on PPD. This study will be the first RCT comparing magnetic bead AA to sham acupressure in alleviating depression and anxiety in new mothers with PPD. Through an RCT design, we aim to gain insight into the effectiveness of magnetic bead AA by minimizing potential biases from confounding variables. For instance, in addition to our use of randomization, our study will also consider potential residual confounding variables that can impact PPD; thus, any positive findings in our study will likely be attributable to the effects of auriculotherapy. In addition, our study utilized seeds with adhesive patches in the sham group, which is different from past studies that have utilized blank patches. Attaching a seed underneath the adhesive patch will help reduce the risk of knowing which intervention was received, thus reducing bias.

Many past studies have only followed participants for the duration of the intervention and were therefore unable to report long-term effects of auriculotherapy. Our study will monitor depression and anxiety symptoms during the 4-week intervention and will also include follow-up at 3 months and 6 months after the start of treatment which will help provide insight into the effects of AA on PPD months after intervention completion. Compared to medical treatments, AA has been found to produce fewer side effects and is inexpensive and non-invasive. The magnetotherapy modality is also convenient and advantageous in this population group since frequent manual pressure to acupoints are not required to create a therapeutic effect.
There are a few limitations to note in our study, such as the single-blinded design. Given the nature of the study, only participants will be blinded, which may cause detection bias. Secondly, our participants are post-vaginal delivery women, which might limit the generalizability of the findings to women giving birth by other methods, such as cesarean section. Lastly, we utilized a single acupressure point instead of multiple acupoints as in some previous studies to verify the effect of Shenmen acupressure on depression and anxiety. We recommend future studies compare the effects of the Shenmen point to different acupoints or even a combination of acupoints to determine which will produce the greatest effect on depression and anxiety in PPD.

4.2 CLINICAL SIGNIFICANCE

Peripartum depression is a prevalent and significant public health issue, with up to 1 in 4 women experiencing depression following childbirth. Treatment for PPD includes psychotherapy and pharmacotherapy; however, cost, side effects, and time constraints are significant barriers to treatment access. In turn, psychotherapy can be expensive, while pharmacotherapy may cause both direct and indirect adverse effects on the infant, and can take up to several weeks to achieve a treatment response. Magnetic bead auricular acupressure has the potential to alleviate symptoms of depression and anxiety in a convenient, cost-effective, and non-invasive manner. This study seeks for an alternative, appealing, and effective treatment option for PPD to prevent progression of PPD, future hospitalizations, suicide, relationship strain, and long-lasting negative effects on infant development. Positive results would add magnetic bead AA as a viable treatment option and open the door for further investigation of alternative and complementary medicine for mothers with PPD.
4.3 REFERENCES


Appendix A: Sample Size Calculation

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>4-week Follow-up</th>
<th>Relative Effect</th>
<th>Standard Deviation</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acupuncture Group</td>
<td>12.79 ± 2.54</td>
<td>7.83 ± 1.65</td>
<td>12.79 – 7.83 = 4.96</td>
<td>$\sqrt{\frac{2.54^2 + 1.65^2}{2}} = 2.14$</td>
<td>4.96 ± 2.14</td>
</tr>
<tr>
<td>Waitlist Control Group for PPD</td>
<td>19.8 ± 5.3</td>
<td>18.3 ± 5.2</td>
<td>19.8 – 18.3 = 1.5</td>
<td>$\sqrt{\frac{5.3^2 + 5.2^2}{2}} = 5.25$</td>
<td>1.5 ± 5.25</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Population Mean</th>
<th>Standard Deviation</th>
<th>N Per Group</th>
<th>Standard Error</th>
<th>99% Lower</th>
<th>99% Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnetic Bead AA</td>
<td>5.0 ± 1</td>
<td>2.1 ± 1</td>
<td>33 ± 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sham AA</td>
<td>1.5 ± 1</td>
<td>5.3 ± 1</td>
<td>33 ± 1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Mean Difference         | 3.5     | 4.0     | 66      | 0.99           | 0.88      | 6.12      |

Alpha = 0.010, Tail = 2

Power: 80%
Type of power analysis
A priori: Compute required sample size - given α, power, and effect size

Input parameters
- Tail(s): Two
- Effect size d: 0.8682431
- α err prob: 0.01
- Power (1-β err prob): 0.8
- Allocation ratio N2/N1: 1

Output parameters
- Noncentrality parameter δ: 3.5268201
- Critical t: 2.6548543
- df: 64
- Sample size group 1: 33
- Sample size group 2: 33
- Total sample size: 66
- Actual power: 0.8048621

Test family
- t tests

Statistical test
- Means: Difference between two independent means (two groups)

n1 ≠ n2
- Mean group 1: 0
- Mean group 2: 1
- SD σ within each group: 0.5

n1 = n2
- Mean group 1: 5.0
- Mean group 2: 1.5
- SD σ group 1: 2.1
- SD σ group 2: 5.3

Calculate
- Effect: 0.8682431

X-Y plot for a range of values
- Calculate

Close effect size drawer
Appendix B: DSM-V Diagnostic Criteria for Peripartum Depression

Note: Peripartum depression is not a separate diagnosis in the DSM-5; instead, patients are diagnosed with major depression with peripartum onset for episodes that arise during pregnancy or within four weeks postpartum.

DSM-5 Diagnostic Criteria for a Major Depressive Episode

| A. 5 (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least 1 of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure. |
| NOTE: Do not include symptoms that are clearly attributable to another medical condition. |
| 1) Depressed mood most of the day, nearly every day, as indicated by either subjective report (eg, feels sad, empty, hopeless) or observations made by others (eg, appears tearful). (NOTE: In children and adolescents, can be irritable mood.) |
| 2) Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation). |
| 3) Significant weight loss when not dieting or weight gain (eg, a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (NOTE: In children, consider failure to make expected weight gain.) |
| 4) Insomnia or hypersomnia nearly every day. |
| 5) Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down). |
| 6) Fatigue or loss of energy nearly every day. |
| 7) Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick). |
| 8) Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by their subjective account or as observed by others). |
| 9) Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide. |

| B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. |

| C. The episode is not attributable to the direct physiological effects of a substance or to another medical condition. |
**NOTE:** Criteria A through C represent a major depressive episode.

**NOTE:** Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgement based on the individual's history and the cultural norms for the expression of distress in the context of loss.

D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.

E. There has never been a manic or hypomanic episode.

**NOTE:** This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.

Appendix C: Consent Form

CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

Title of Study: Auricular Acupressure on Depression and Anxiety in Mothers with Peripartum Depression  
Principal Investigator: Kieran O’Donnell, PhD  
Co-Investigator: Jane Chan, PA-SII  
Affiliation: Yale New Haven Health System and Yale School of Medicine

Invitation to Participate and Study Purpose

We would like to extend an invitation to participate in our study of magnetic bead auricular acupressure for peripartum depression. You have been referred because you have been diagnosed with peripartum depression. The current study will enroll 70 total participants from the greater Yale New Haven Health System. Active participation in the study will require a total of 6 months from enrollment and baseline assessments to the last follow-up.

To decide your willingness to participate, please continue to read the following details about the study. A research staff member will then review the purpose, procedures, risks, and benefits of the study and to make sure that all questions or concerns are addressed.

Description of Study and Procedures

Enrollment in this study requires that you meet set inclusion and exclusion criteria. These criteria are as follows:

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Mothers aged 18-45</td>
<td>• Trauma or inflammation of either pinna</td>
</tr>
<tr>
<td>• Primiparous women</td>
<td>• Suicidal ideation</td>
</tr>
<tr>
<td>• Vaginal delivery within 6 months</td>
<td>• Thoughts of harming their baby</td>
</tr>
<tr>
<td>• Delivery of a healthy infant (at least 36 weeks gestation)</td>
<td>• Current or past diagnosis of bipolar disorder, schizophrenia, or other psychotic disorder</td>
</tr>
<tr>
<td>• PHQ-9 score of $\geq$ 10</td>
<td>• Current psychotic symptoms</td>
</tr>
<tr>
<td>(predictive of Major Depressive Disorder)</td>
<td>• Substance use disorder</td>
</tr>
<tr>
<td></td>
<td>• Current illegal drug use (based on self-report or positive urine screen)</td>
</tr>
<tr>
<td></td>
<td>• Current use of antidepressants, anxiolytics, antipsychotics, acupuncture/acupressure, or other complementary and alternative medicine</td>
</tr>
<tr>
<td></td>
<td>• Ongoing treatment with psychotherapy</td>
</tr>
</tbody>
</table>
A written informed consent form (this document) is to be signed by both you, the participant, and the Primary Investigator (Dr. Kieran O’Donnell) or Co-Investigator (Jane Chan, PA-SII). The purpose of this informed consent is to outline the study purpose and study designs so that you will understand your responsibilities as a participant in the study. Enrollment in this study is optional. Once enrolled, you may discontinue your enrollments at any time with notification to the PI.

Following enrollment in the study, additional demographic and pertinent medical history will be obtained regarding your diagnosis of peripartum depression. We will also require a detailed list of your current medications and may request additional information of relevant family medical history. If needed, we may request that you provide medical records from doctors who manage your peripartum depression. This study is HIPAA compliant so that no personal identification information will be associated with the study documents completed as a result of your participation.

During your participation in this study, you will complete written evaluations and participate in online video interviews with a psychiatrist. These assessments will be performed at five different instances throughout the 6-month period with the goal to assess and follow-up on your depression and anxiety symptoms at that time.

You will be assigned to one of two treatment groups by a random process such that each group will have an equal number of participants with similar degrees of peripartum depression. One treatment group will receive magnetic bead auricular acupressure and the other group will receive sham auricular acupressure. Each group will meet with the acupuncturist at the beginning of each week for ear patch placement, for a total of 4 weeks. Details of these therapies will be explained in full prior to and at the treatment sessions. You will be required to attend each treatment session, and the need to make up sessions will be evaluated on a case-by-case basis.

In the case that you miss more than 1 treatment session, you will be automatically un-enrolled from the study.

Below is a flow chart indicating the activities that will occur at each visit:
Risks or Inconveniences

This study is deemed low to no risk. Adverse effects from magnetic bead auricular acupressure may include skin damage, infection, and allergic reaction. These risks are rare, however, in the event that they do occur, the study team will cease the allocated intervention and provide appropriate treatment.

Expected Benefits

Magnetic bead auricular acupressure may improve depression and anxiety symptoms. It may also benefit mood, concentration, sleep quality, and relationship with the infant.

Economic Considerations

There will be no costs for participation in the study; however, there will also be no paid reward for enrollment in the study.
Confidentiality of Information

Any identified information obtained or reviewed in this study will remain confidential and only disclosed as required by the United States or Connecticut law. Only the parties listed in the research authorization form attached will be granted access to identifiable information we collect. When the study is published, there will be no information that will link your identity to the study unless you give specific permission to disclose personal information.

Research Subject’s Rights:

You are able to decline enrollment into the study and may discontinue participation at any point throughout the study. However, any data gathered prior to withdrawing participation may still be used in the study analyses to ensure study integrity and study oversight. There will be no penalty or loss of benefits associated with withdrawal of participation. The quality of medical care that you will receive will not be affected by choice to participate in this study. Please notify the Primary Investigator, Dr. Kieran O’Donnell or Co-Investigator, Jane Chan, PA-II, with a written notice if you choose to withdraw.

Authorization

I have read (or have been read) this form and have decided to participate in the project described. The general purpose, risks, and benefits are clear and acceptable to me.

By signing this form, I give permission to researchers to use information about myself for the purposes described in this form. By declining participation, I understand that I will not receive the therapies in this study.

Name of Participant (Print): ______________________

Signature of Participant: ______________________ Date: ________________

Name of Person Obtaining Consent (Print): ______________________

Signature of Person Obtaining Consent: ________________ Date: ________________

Any further questions or concerns about this research project may be directed to the Principal Investigator: Dr. Kieran O’Donnell (kieran.odonnell@yale.edu)

If you have any questions after signing this form about your privacy rights, please contact the Yale Privacy Officer at 203-432-5919.

If you have questions about your rights as a research participant, or have complaints about this research, you can contact the Yale Institutional Review Boards at 203-785-4688 or email hrpp@yale.edu.

YALE UNIVERSITY
RESEARCH AUTHORIZATION

Subject Name: ________________  Medical Record #: ____________

Principal Investigator: __________  IRB #: __________________

Principal Investigator’s Contact Information: ______________________

To the Subject:

The health-related information that we gather about you in this study is personal. The Yale School of Medicine and the Yale New Haven Health System researchers are required by law to protect the privacy of the information known as protected health information or PHI. All reasonable efforts will be made to protect the confidentiality of your PHI, which may be shared with others to support this research, to conduct public health reporting, and to comply with the law as required. Despite these protections, there is a possibility that information about you could be used or disclosed in a way that it will no longer be protected by federal law. For example, some of the individuals listed on page 2 of this form may not be required by law to meet HIPAA standards for privacy of health information. These individuals or companies are nonetheless required through other agreements with Yale to keep your information confidential.

In this form, we describe who will be working with this information and ask for your permission to use the information in the research study.

Please read this form carefully. If you have any questions, please ask the Principal Investigator listed above before signing this form.

By signing this form, you give permission for the researchers to use and/or disclosure the information as described below, for this research study. The reason for the uses and disclosures is to assess magnetic bead auricular acupressure on peripartum depression.

You have a right to refuse to sign this form. Your health care outside the study, the payment for your health care, and your health care benefits will not be affected if you do not sign this form.

If you do not sign this form, you will not be able to enter this research study and will not receive treatment as a study participant.

If you sign this form, you may change your mind at any time, but the researchers may still use the information collected before you changed your mind in order to complete the research.

This form will never expire unless and until you change your mind and retract it. To retract the permission to use your information, please tell the study staff or write to Dr. Kieran O’Donnell or Jane Chan, PA-SII.
You will not be allowed to see or copy the part of your medical records that describe a research treatment until the research is completed, but you may see and copy the research treatment information at the end of the research in agreement with institutional medical record policies.

You have a right to receive a copy of this form after you have signed it. If you have any questions about your rights after you have signed this form, please contact the Yale Privacy Officer at 203-436-3650.

Use and Disclosure Covered by this Authorization

(1) Who will disclose, receive, and/or use the information?

The following person(s), class(es) of persons, and/or organization(s) may share, use, and receive the information listed below in connection with this study. These persons are authorized to use and disclose the information to the other parties on this list, to you or your personal representative, or as permitted by law.

☐ The following health care facilities or research site(s) and research staff involved in this study: **Yale New Haven Health System, Yale School of Medicine, Research Investigators, Clinical Research Assistants**

☐ Health care providers who referred and connected you to this study

☐ Laboratories and other individuals and organizations that analyze your health information in connection with this study, in accordance with the study’s protocol

☐ The members and staff of the Human Investigation Committee that approved this study

☐ Those individuals at Yale who are responsible for the financial oversight of research including billings and payments

☐ Principal Investigator: Dr. Kieran O’Donnell

☐ Additional members of the Research Team

☐ Data and Safety Monitoring Boards and others authorized to monitor the conduct of the study

☐ Others (as described below)

(2) What personal health information will be used or disclosed?

The following information about you may be used and disclosed:
☐ Research study records

☐ Medical and laboratory records of only those services provided in connection with this study

☐ The entire research record and any medical records held by the Yale New Haven Health System centers with peripartum depression diagnosis from: _____ to: _____

☐ The following information:

Signature

I have read this form and all of my questions about this form have been answered. By signing below, I authorize the described uses and disclosures of information.

________________________________________
Signature of Subject or Personal Representative

________________________________________
Print Name of Subject or Personal Representative

________________________________________
Date

Description of Personal Representative’s Authority

THE SUBJECT OR HIS OR HER PERSONAL REPRESENTATIVE MUST BE PROVIDED WITH A COPY OF THIS FORM AFTER IT HAS BEEN SIGNED

Reviewed and Acknowledged

________________________________________
Human Investigation Committee
Yale University

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Appendix D: Hamilton Depression Rating Scale (HAMD-17)

### Hamilton Depression Rating Scale (HDRS)

**PLEASE COMPLETE THE SCALE BASED ON A STRUCTURED INTERVIEW**

**Instructions:** For each item select the one “cue” which best characterizes the patient. Be sure to record the answers in the appropriate spaces (positions 0 through 4).

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DEPRESSED MOOD (sadness, hopelessness, helplessness, worthlessness)</td>
<td>6 Absent. 1 These feelings indicated only on questioning. 2 These feelings spontaneously reported verbally. 3 Communicates feelings non-verbally, i.e., through facial expression, posture, voice and tendency to weep. 4 Patient reports virtually only these feelings in his/her spontaneous verbal and non-verbal communication.</td>
</tr>
<tr>
<td>2</td>
<td>FEELINGS OF GUILT</td>
<td>0 Absent 1 Self-reproach, feels he/she has let people down. 2 Ideas of guilt or rumination over past errors or sinful deeds. 3 Present illness is a punishment. Delusions of guilt. 4 Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations.</td>
</tr>
<tr>
<td>3</td>
<td>SUICIDE</td>
<td>0 Absent 1 Feels life is not worth living. 2 Wishes he/she were dead or any thoughts of possible death to self. 3 Ideas or gestures of suicide. 4 Attempts at suicide (any serious attempt rate 4).</td>
</tr>
<tr>
<td>4</td>
<td>INSOMNIA: EARLY IN THE NIGHT</td>
<td>0 No difficulty falling asleep. 1 Complains of occasional difficulty falling asleep, i.e., more than 1/2 hour. 2 Complains of nightly difficulty falling asleep.</td>
</tr>
<tr>
<td>5</td>
<td>INSOMNIA: MIDDLE OF THE NIGHT</td>
<td>0 No difficulty. 1 Patient complains of being restless and disturbed during the night. 2 Waking during the night – any getting out of bed rates 2 (except for purposes of voiding).</td>
</tr>
<tr>
<td>6</td>
<td>INSOMNIA: EARLY HOURS OF THE MORNING</td>
<td>0 No difficulty. 1 Waking in early hours of the morning but goes back to sleep. 2 Unable to fall asleep again if he/she gets out of bed.</td>
</tr>
<tr>
<td>7</td>
<td>WORK AND ACTIVITIES</td>
<td>0 No difficulty. 1 Thoughts and feelings of incapacity, fatigue or weariness related to activities, work or hobbies. 2 Loss of interest in activity, hobbies or work – either directly reported by the patient or indirect in listlessness, indecision and vacillation (feels he/she has to push self to work or activities). 3 Decrease in actual time spent in activities or decrease in productivity. Rate 3 if the patient does not spend at least three hours a day in activities (job or hobbies) excluding routine chores. 4 Stopped working because of present illness. Rate 4 if patient engages in no activities except routine chores, or if patient fails to perform routine chores unassisted.</td>
</tr>
<tr>
<td>8</td>
<td>ANXIETY SOMATIC (physiological concomitants of anxiety) such as: gastro-intestinal – dry mouth, wind, indigestion, diarrhea, cramps, belching cardiovascular – palpitations, headaches respiratory – hyperventilation, sighing urinary frequency sweating</td>
<td>0 Absent 1 Mild 2 Moderate 3 Severe 4 Incapacitating.</td>
</tr>
<tr>
<td>9</td>
<td>SOMATIC SYMPTOMS GASTRO-INTESTINAL</td>
<td>0 None. 1 Loss of appetite but eating without staff encouragement. Heavy feelings in abdomen. 2 Difficulty eating without staff urging. Requests or requires laxatives or medication for bowels or medication for gastro-intestinal symptoms.</td>
</tr>
<tr>
<td>10</td>
<td>GENERAL SOMATIC SYMPTOMS</td>
<td>0 None. 1 Heaviness in limbs, back or head. Backaches, headaches, muscle aches. Loss of energy and fatigability. 2 Any clear-cut symptom rates 2.</td>
</tr>
<tr>
<td>11</td>
<td>GENITAL SYMPTOMS (symptoms such as loss of libido, menstrual disturbances)</td>
<td>0 Absent 1 Mild 2 Severe.</td>
</tr>
<tr>
<td>12</td>
<td>HYPOCHONDRIASIS</td>
<td>0 Not present 1 Self-absorption (bodily). 2 Preoccupation with health. 3 Frequent complaints, requests for help, etc. 4 Hypochondriacal delusions.</td>
</tr>
</tbody>
</table>
8 RETARDATION (slowness of thought and speech, impaired ability to concentrate, decreased motor activity)
   0 [] Normal speech and thought.
   1 [] Slight retardation during the interview.
   2 [] Obvious retardation during the interview.
   3 [] Interview difficult.
   4 [] Complete stupor.

9 AGITATION
   0 [] None.
   1 [] Fidgetiness.
   2 [] Playing with hands, hair, etc.
   3 [] Moving about, can’t sit still.
   4 [] Hand wringing, nail biting, hair-pulling, biting of lips.

10 ANXIETY PSYCHIC
   0 [] No difficulty.
   1 [] Subjective tension and irritability.
   2 [] Worrying about minor matters.
   3 [] Apprehensive attitude apparent in face or speech.
   4 [] Fears expressed without questioning.

16 LOSS OF WEIGHT (RATE EITHER a OR b)
   a) According to the patient: measurements:
      0 [] No weight loss
      1 [] Less than 1 lb weight loss in week.
      2 [] Greater than 1 lb weight loss in week.
   b) According to weekly present illness.
      0 [] No weight loss
      1 [] Less than 1 lb weight loss
      2 [] Greater than 2 lb weight loss
      3 [] Not assessed.

17 INSIGHT
   0 [] Acknowledges being depressed and ill.
   1 [] Acknowledges illness but attributes cause to bad food, climate, over-work, virus, need for rest, etc.
   2 [] Denies being ill at all.

Total score: _____
Appendix E: Demographic Survey

Demographic Survey

Name: ___________________________                Today’s date: _______________

1. Date of birth: ____ / ____ / ____
2. Height: _____ ft _____ in
3. Weight: _____ lbs

Please circle your answer for the following questions:

4. Race or ethnicity
   a. White
   b. Black or African American
   c. Asian
   d. Hispanic or Latino
   e. Other: __________________

5. Highest education level
   a. Never school
   b. Primary school
   c. Middle school
   d. High school
   e. College or above

6. Occupation
   a. Unemployed
   b. Employed
   c. Self-employed
   d. Student

7. Marital status
   a. Single
   b. Married
   c. Divorced/separated
   d. Widowed

8. Household Income
   a. ≤ $20,000
   b. $20,001-$40,000
   c. $40,001-$60,000
   d. $80,001-$1000,000
   e. ≥ $100,000
Appendix F: General Anxiety Disorder (GAD-7) Questionnaire

GAD-7 Anxiety

<table>
<thead>
<tr>
<th>Over the last two weeks, how often have you been bothered by the following problems?</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Feeling nervous, anxious, or on edge</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Not being able to stop or control worrying</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Worrying too much about different things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Trouble relaxing</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Being so restless that it is hard to sit still</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Becoming easily annoyed or irritable</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Feeling afraid, as if something awful might happen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Column totals

Total score

If you checked any problems, how difficult have they made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all | Somewhat difficult | Very difficult | Extremely difficult
---|---|---|---
[ ] | [ ] | [ ] | [ ]
Appendix G: Edinburgh Postnatal Depression Scale (EPDS)

Edinburgh Postnatal Depression Scale\(^1\) (EPDS)

<table>
<thead>
<tr>
<th>Name: ___________________________</th>
<th>Address: ___________________________</th>
</tr>
</thead>
<tbody>
<tr>
<td>Your Date of Birth: ___________________________</td>
<td>Phone: ___________________________</td>
</tr>
<tr>
<td>Baby’s Date of Birth: ___________________________</td>
<td>Phone: ___________________________</td>
</tr>
</tbody>
</table>

As you are pregnant or have recently had a baby, we would like to know how you are feeling. Please check the answer that comes closest to how you have felt IN THE PAST 7 DAYS, not just how you feel today.

Here is an example, already completed.

I have felt happy:
- Yes, all the time
- Yes, most of the time  This would mean: “I have felt happy most of the time” during the past week.
- No, not very often  Please complete the other questions in the same way.
- No, not at all

In the past 7 days:

1. I have been able to laugh and see the funny side of things
   - As much as I always could
   - Not quite so much now
   - Definitely not so much now
   - Not at all

2. I have looked forward with enjoyment to things
   - As much as I ever did
   - Rather less than I used to
   - Definitely less than I used to
   - Hardly at all

3. I have blamed myself unnecessarily when things went wrong
   - Yes, most of the time
   - Yes, some of the time
   - Not very often
   - No, never

4. I have been anxious or worried for no good reason
   - No, not at all
   - Hardly ever
   - Yes, sometimes
   - Yes, very often

5. I have felt scared or panicly for no very good reason
   - Yes, quite a lot
   - Yes, sometimes
   - No, not much
   - No, not at all

6. Things have been getting on top of me
   - Yes, most of the time I haven’t been able to cope at all
   - Yes, sometimes I haven’t been coping as well as usual
   - No, most of the time I have coped quite well
   - No, I have been coping as well as ever

7. I have been so unhappy that I have had difficulty sleeping
   - Yes, most of the time
   - Yes, sometimes
   - Not very often
   - No, not at all

8. I have felt sad or miserable
   - Yes, most of the time
   - Yes, quite often
   - Not very often
   - No, not at all

9. I have been so unhappy that I have been crying
   - Yes, most of the time
   - Yes, quite often
   - Only occasionally
   - No, never

10. The thought of harming myself has occurred to me
    - Yes, quite often
    - Sometimes
    - Hardly ever
    - Never


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