The Efficacy of Probiotic Intervention in Improving Mood

Laura Ramsey

Samantha Stern

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The Efficacy of Probiotic Intervention in Improving Mood

Abstract

**Background:** Mood disorders are a significant public health concern. Recent studies have shown a connection between healthy gut flora and mood. Due to the overwhelming association between poor gut flora health and common mood disorders, many providers are turning to probiotics as a safe, affordable, and effective therapy for their patients. This review will investigate the utility of probiotics on mood.

**Methods:** An exhaustive literature search using MEDLINE-Ovid, Web of Science, CINAHL, and Research Gate was conducted. The following search terms were used: “probiotics” and “mood disorders.” The bibliographies from several relevant background articles were used and inclusion and exclusion criteria were applied.

**Results:** The initial search yielded 39 articles for review. After eliminating duplicates and screening these results for relevant articles using eligibility criteria, there were a total of 2 articles. Study 1 was a randomized, triple-blind study, and Study 2 was a randomized, double-blind study. Two other randomized double-blind articles were excluded based on the population that was studied or the primary outcome did not include mood response. Both studies resulted in a significant improvement in mood after the use of probiotics.

**Conclusion:** Probiotics have the potential to be used to improve mood in a generally healthy population. Further studies are required in order to determine the mechanism of probiotics on mood. The importance in further understanding probiotics stems from the potential to provide a safe, affordable, and effective therapy to help generally healthy patients improve mental health and well being. Once an understanding of probiotics on the mood of healthy individuals is achieved, this may be applied to individuals with specific mood disorders.

**Keywords:** Probiotics and mood disorders

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The Efficacy of Probiotic Intervention in Improving Mood

Laura Ramsey and Samantha Stern

A Clinical Graduate Project Submitted to the Faculty of the
School of Physician Assistant Studies
Pacific University
Hillsboro, OR

For the Masters of Science Degree, August 12, 2017

Clinical Graduate Project Coordinator: Annjanette Sommers, PA-C, MS
Biography

Laura Ramsey was born and raised in St. Paul, Minnesota. She obtained a Bachelor's degree in Biology and Global Health at the University of Wisconsin-Madison. After graduation she travelled through southern Africa and worked at the University of Cape Town’s Groote Schuur Hospital researching rheumatic heart disease. It was during this time she decided to pursue a career as a Physician Assistant. She then moved to Honolulu, Hawaii and worked as an anesthesia technologist at Straub Hospital to gain medical experience and patient contact hours before applying to PA school. After PA school she plans to make the Pacific Northwest her home, while continuing to travel internationally.

Sammie Stern was born and raised in Mequon, WI. After deciding that she wanted to become a Physician Assistant, she switched her undergraduate studies at the University of Minnesota from business to Biology. After graduation she traveled to South Africa to work in various underserved hospitals in order to complete her senior thesis. After returning, she moved to Lake Tahoe and worked as a medical assistant at the medical clinic on Squaw Valley before beginning PA school. She is hoping to spend her career working internationally and in integrative medicine.
Abstract

Background: Mood disorders are a significant public health concern. Recent studies have shown a connection between healthy gut flora and mood. Due to the overwhelming association between poor gut flora health and common mood disorders, many providers are turning to probiotics as a safe, affordable, and effective therapy for their patients. This review will investigate the utility of probiotics on mood.

Methods: An exhaustive literature search using MEDLINE-Ovid, Web of Science, CINAHL, and Research Gate was conducted. The following search terms were used: “probiotics” and “mood disorders.” The bibliographies from several relevant background articles were used and inclusion and exclusion criteria were applied.

Results: The initial search yielded 39 articles for review. After eliminating duplicates and screening these results for relevant articles using eligibility criteria, there were a total of 2 articles. Study 1 was a randomized, triple-blind study, and Study 2 was a randomized, double-blind study. Two other randomized double-blind articles were excluded based on the population that was studied or the primary outcome did not include mood response. Both studies resulted in a significant improvement in mood after the use of probiotics.

Conclusion: Probiotics have the potential to be used to improve mood in a generally healthy population. Further studies are required in order to determine the mechanism of probiotics on mood. The importance in further understanding probiotics stems from the potential to provide a safe, affordable, and effective therapy to help generally healthy patients improve mental health and well being. Once an understanding of probiotics on the mood of healthy individuals is achieved, this may be applied to individuals with specific mood disorders.

Keywords: Probiotics and mood disorders
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Table I: Quality Assessment of Reviewed Articles

Table II: Study 1: Summary of Findings

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List of Abbreviations

GI  Gastrointestinal
IBD  Irritable bowel disease
WHO  World Health Organization
LEIDS  Leiden Index of Depression Sensitivity Scale
BDI  Beck Depression Inventory
BAI  Beck Anxiety Inventory
GHQ  General Health Questionnaire
DASS       Depression Anxiety and Stress Scale
The Efficacy of Probiotic Intervention in Improving Mood

BACKGROUND

Mood disorders are a significant health problem in the United States. According to the National Institute of Mental Health\textsuperscript{12}, 40 million adults age 18 and older are affected by mood disorders. One study\textsuperscript{6} found that the lifetime prevalence for developing a mood disorder meeting DSM-IV criteria are estimated to be 20.8\%. This does not include the many individuals who suffer from undiagnosed or subclinical symptoms. Mood disorders can have widespread effects on society by affecting the sufferer’s individual life, work, and relationships. Despite the incredible prevalence, the source of many mood disorders remains unknown. As such, prevention remains limited. In addition, treatment of existing disorders can be incredibly complex, often involving cognitive behavioral therapy and pharmacologic intervention. Prescription interventions can become a great financial burden and with undesirable side effects. This often leaves the medical provider seeking alternative methods to help their patients.

Utilizing probiotics to change the health of the gut and gut barrier is a new area of research and the clinical world is just beginning to understand the potential importance of this connection. Probiotics are defined by the World Health Organization (WHO) as live microorganisms that, when administered in adequate amounts, confer a health benefit to
the host. While their mechanism of action is not completely understood, major mechanisms by which probiotics are thought to act include inhibiting the growth or expression of bacterial virulence factors, preventing colonization with pathogenic bacteria, modulation of one or more mucosal and/or systemic immune responses, and improving gastrointestinal barrier integrity.

Specifically, studies have shown that bacteria in the gastrointestinal (GI) tract interact with the vagus nerve. Activated vagal sensory neurons send information about stimuli within the GI tract to the brain, which can be integrated with ongoing imbalanced emotional states and behavior. An underlying bacterial infection or imbalance in gut flora has been associated with increased pro-inflammatory cytokines, anxiety, and other mood and affective changes.

Gut flora imbalance also influences the protective epithelial gut barrier. Compromised integrity of the epithelial barrier has been associated with increased pro-inflammatory cytokine levels and a wide range of intestinal and systemic diseases, including allergies, autoimmune disorders, asthma, inflammatory bowel disease (IBD), poor mental health, stress, and fatigue.

As such, the paper will focus on the effects of probiotics on the mood of patients considered generally healthy.

METHODS

An exhaustive literature search of available medical literature was performed using MEDLINE-Ovid, Web of Science, CINAHL, and Research Gate. The following
search terms were used: “probiotics” and “mood disorders.” The bibliographies from several relevant background articles were used and inclusion and exclusion criteria were applied. Included were studies conducted on healthy populations, evaluating oral probiotic therapy in comparison to a placebo and measuring mood response as a primary outcome. Studies were excluded if mood response was not a primary outcome or if the population studied had a prior-diagnosed mental health disorder. Relevant articles were assessed for quality using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE)\(^1\).

**RESULTS**

The initial search yielded 39 articles for review. After screening the articles using eligibility criteria, a total of two articles were assessed for this systematic review (See Table 1).

**Study 1: Steenbergen et al 2015**

This 4-week triple-blind, randomized control trial\(^11\) was designed to compare the effect of multispecies probiotics to inert placebo in 40 healthy participants without current mood disorders. Participants received a food supplementation containing a placebo or the following strains: *bifidobacterium bifidum* W23, *bifidobacterium lactis* W52, *lactobacillus acidophilus* W37, *lactobacillus brevis* W63, *L. casei* W56, *lactobacillus salivarius* W24, and *lactococcus lactis* W19 and W58. The participants were then provided a pre- and post-intervention assessment and cognitive reactivity to sad
mood was assessed using the revised Leiden Index of Depression Sensitivity Scale (LEIDS), the Beck Depression Inventory (BDI), and the Beck Anxiety Inventory (BAI). LEIDS scores have been found to predict depression incidence in multiple longitudinal studies assessing aggression, hopelessness/suicidality, acceptance/coping, control/perfectionism, risk aversion, and rumination. The BDI has been found to be a valid indicator of depression and show good diagnostic discrimination. The BAI assesses the existence and severity of anxiety symptoms.

This study demonstrated that a 4-week multispecies probiotic intervention has a positive effect (see table 2) on cognitive reactivity to naturally occurring changes in sad mood in healthy individuals not currently diagnosed with a depressive disorder. More specifically, the probiotic intervention reduced aggressive and ruminative thoughts in response to sad mood. Therefore, probiotics may be a safe and natural alternative to prevent depression.

Study 2: Mohammadi et al 2015

In this study, a randomized double-blind, placebo-controlled trial was conducted on 70 petrochemical workers. Subjects were randomly divided into 3 groups to receive 100 g/day probiotic yogurt + one placebo capsule (n = 25) or one probiotic capsule daily + 100 g/day conventional yogurt (n = 25) or 100 g/day conventional yogurt + one placebo capsule (n = 20) for 6 weeks. Mental health parameters including general health questionnaire (GHQ) and depression anxiety and stress scale (DASS) scores were measured.
In analyzing the design of this study, participants were requested to not change their routine physical activity or usual dietary intakes throughout the study. Participants were also requested to not consume any probiotic or synbiotic products other than those provided by the study. All participants provided 3 dietary records throughout the intervention and 3 physical activity records to make sure that they maintained their usual diet and physical activity during the study\textsuperscript{9}.

After 6 weeks of intervention, a significant improvement of GHQ and DASS was observed in the probiotic yogurt and probiotic capsule groups. There was no significant improvement seen in the conventional yogurt group. The study concluded that the consumption of probiotic yogurt or a multispecies probiotic capsule had beneficial effects on mental health parameters in petrochemical workers\textsuperscript{9}.

**DISCUSSION**

The global prevalence of mood disorders has led to an emphasis on new research outlining preventative and management therapy. The theory that gut bacteria can impact mental health has opened doors to alternative therapies that will hopefully be able to provide safer and more affordable therapy alternatives. The focus of this systematic review was to determine the association of probiotics and the effect on the general population's mood.
This systematic review was able to uncover two studies\textsuperscript{9,11} that looked at the effect of probiotics on mood. Both studies\textsuperscript{9,11} agreed that consumption of probiotics improved mood in healthy participants. This is an incredible finding for medical providers of patients with mood disorders who struggle to find safe, affordable, and effective treatment for their ailments. However, further research is required to determine the exact mechanism of action of probiotics on mood in diverse populations.

Limitations of Study 1 (Steenbergen et al)\textsuperscript{11} include a small sample size and a lack of monitoring for intake of other probiotic products or fermented foods by the participants. In addition, the compliance of the participants was solely facilitated by text message reminders and not further confirmed by stool bacterial analysis. The participants of the study were predominantly young adult females, which limits the utility of the study from being applied to the general population. Study 2 (Mohammadi et al study)\textsuperscript{9} is limited by its failure to include participant demographics. In addition, the sample size is small and confined to petrochemical workers of one location.

Two other studies\textsuperscript{2,10} were considered that also agreed with this outcome. However, one study\textsuperscript{2} was excluded because the main objective was not to improve mood, this was solely a secondary finding to the administration of a milk drink to subjects. The other study\textsuperscript{10} was excluded because the population of the study was already considered to be sick with chronic fatigue syndrome.

Probiotics have a promising potential to be used to improve mood in a generally healthy population. Although further research is necessary to solidify the exact
mechanisms of probiotics and how they correlate to improvement in mood, it has been well established that the gut microbiota is intimately connected via the brain-gut axis and plays a role in neural, endocrine, and immune pathways\(^4\). The importance in further understanding probiotics stems from them providing a means to safe, affordable, and effective therapy to help patients improve mental health and well being.

**CONCLUSION**

Probiotics are a safe and highly advisable therapy for medical providers to recommend to patients seeking to improve mood and wellbeing. Probiotics are a low-risk and affordable therapy that should be considered for patients who are at risk for mood disorders. While this study investigated the effects of probiotics on the mood of generally healthy participants, the utility of probiotics to prevent and treat mood disruption in patients with already diagnosed mood disorders is an exciting possibility in the not too distant future.
References


### Table I: Quality Assessment of Reviewed Articles

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Downgrade Criteria</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1 (Steenbergen et al)</td>
<td>RCT</td>
<td>Serious*</td>
</tr>
<tr>
<td>Study 2 (Mohammadi et al)</td>
<td>RCT</td>
<td>Very serious†</td>
</tr>
</tbody>
</table>

* Small sample size
† Studied only petrochemical workers

### Table II: Study 1: Summary of Findings

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEIDS-r</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>44.70</td>
<td>42.30</td>
</tr>
<tr>
<td>Probiotics</td>
<td>42.75</td>
<td>33.35</td>
</tr>
<tr>
<td>BDI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>9.10</td>
<td>9.10</td>
</tr>
<tr>
<td>Probiotics</td>
<td>7.90</td>
<td>7.25</td>
</tr>
<tr>
<td>BAI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>12.21</td>
<td>11.21</td>
</tr>
<tr>
<td>Probiotics</td>
<td>11.35</td>
<td>9.95</td>
</tr>
</tbody>
</table>

Mean pre- and post-intervention scores on the LEIDS-r, BDI, and BAI in the Placebo and Probiotics groups. In each questionnaire, participants were presented with symptoms relating to depression or anxiety and asked to indicate on a scale (0, not at all, 1, mildly, 2, moderately, 3, severely, etc.) that best described how they have been feeling. The total scores may vary between the studies. Total scores are obtained by summing all items.

### Table III: Study 2: Summary of Findings

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHQ Scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conventional yogurt</td>
<td>19.3 +/- 1.5</td>
<td>16.0 +/- 1.9</td>
<td>-3.3 +/- 1.7</td>
</tr>
<tr>
<td>Probiotic yogurt</td>
<td>18.0 +/- 1.5</td>
<td>13.5 +/- 1.9</td>
<td>-4.5 +/- 1.7</td>
</tr>
<tr>
<td>Probiotic capsule</td>
<td>16.9 +/- 1.8</td>
<td>9.8 +/- 1.9</td>
<td>-7.1 +/- 1.7</td>
</tr>
<tr>
<td>DASS scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conventional yogurt</td>
<td>28.4 +/- 4.4</td>
<td>21.7 +/- 4.6</td>
<td>-6.7 +/- 3.3</td>
</tr>
<tr>
<td>Probiotic yogurt</td>
<td>23.3 +/- 3.7</td>
<td>13.0 +/- 3.7</td>
<td>-10.3 +/- 3.9</td>
</tr>
<tr>
<td>Probiotic capsule</td>
<td>18.9 +/- 3.2</td>
<td>9.4 +/- 4.0</td>
<td>-9.5 +/- 4.3</td>
</tr>
</tbody>
</table>

The GHQ-28 comprises 28 items consisting of four subscales: somatic symptoms, anxiety and insomnia, social dysfunction, and severe depression. The DASS questionnaire consists of three 14-times self-report scales the measure depression, anxiety, and stress.