

Yeast based spreads Improve Anxiety and Stress

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Abstract

Yeast based spreads (YBS) such as marmite and vegemite, made from leftover brewer's yeast extract are one of the world's richest source of B vitamins. We evaluated symptoms of depression, anxiety, stress scores (DASS) in participants who consume or do not consume YBS. 520 participants completed a survey consisting of 70-94 questions relating to the consumption of YBS, dietary and lifestyle habits and mood symptoms of DASS. Parametric analysis co-varying for gender, diet, supplement use, soy milk and alcohol consumption and history of psychiatric disorders including depression and anxiety were utilized to analyse the results. A significant improvement was noted in anxiety and stress but not depressive symptoms in those consuming YBS. Furthermore, those who consumed vitamin B12 fortified YBS showed even greater improvement in stress symptomology. Vitamin B supplementation appears to be an important additive supplementary source to improved stress and anxiety in the general adult population

Keywords

Yeast based spreads; Anxiety; Stress; Depression; Vitamin B; Vitamin B12; DASS

1. Introduction

The global incidence of major depressive disorder will be second only to heart disease as the leading cause of death and disability in the next 20 years (Murray & Lopez, 1997; Whitecloudfoundation, 2014). Depression and frequently associated anxiety places a significant load on the economy with the global cost of mental illness, estimated at \$2.5 trillion in 2010, anticipated to increase to over \$6 trillion by 2030 (Who press, 2008). People experiencing major depressive disorder typically present with sadness and/or loss of pleasure in previously enjoyed activities for at least two weeks. Typically an episode of depression is also associated with a sense of worthlessness and guilt, cognitive, sleep and appetite disturbance and often thoughts of suicide or death (Beyondblue, 2014). A major depressive disorder can present slightly differently in children and young adults with a greater propensity to agitation and aggressive outbursts (Burns & Birrell, 2014). The highest risk of completed suicide in Australia (7 per day) occurs in people between 15-45 years (Beyondblue, 2014). Biopsychosocial determinants of depression include genetic and biochemical factors as well as illness and significant life events and psychological trauma. Many neurochemical pathways linked to cognitive function including, glutamate and GABA neurotransmitter systems, serotonergic, noradrenergic, dopaminergic and cholinergic systems, may contribute to depression when there is an aberration of usual function (Dale, Bang-Andersen, & Sanchez, 2015; Mann, 1999; Meldrum, 2000; Niciu, Kelmendi, & Sanacora, 2012; Ressler & Nemeroff, 2000; Sullivan, Coplan, Kent, & Gorman, 1999; van Stegeren, 2008; Yadid & Friedman, 2008). B vitamins play an important role in these neurochemical pathways as significant contributors to neuronal function.

Depression and anxiety, although clinically different conditions, will often co-occur. More than half of the people diagnosed with depression will also experience symptoms of anxiety and vice versa (Beyondblue, 2014). Anxiety disorders as distinct from depression, are characterised by autonomic hyperarousal and subsequent fatigue (increasing illness risk) demonstrated in an archetypal fear response which include escape and avoidance behaviours, , perception of imminent and future threat, anxiety and tension that may exist within or outside the anxiety provoking situation (Craske et al., 2009). In light of this shared vulnerability and comorbidity it may be important to be searching for simple

nutritional strategies at a population health level that might improve depression and anxiety symptoms. This report investigates the potential of a rich vitamin B source to improve mood and anxiety in people who experience some symptoms of these mood states but not as replacement for the pharmacological treatment of full blown mood and anxiety disorders.

Vitamins play a major role in health and are integral for many metabolic functions within the body including correct performance of the methylation cycle, monoamine oxidase production, DNA synthesis, repair and maintenance of phospholipids, and conservation of proper cognitive function. The role of Monoamine oxidase is to inactivate neurotransmitters and a dysfunction in this role is considered to cause several psychiatric and neurological disorders, including depression. Likewise, medications that decrease the activity of MOA are proven antidepressants used to increase serotonin bioavailability. A deficiency of B vitamins caused by dietary inadequacy or absorption defects, could influence memory function and cognitive impairment and dementia. Vitamins that have been predominantly linked to neuronal function include vitamins B1, B3, B6, B9 and B12, and deficiencies have been linked to neurological disorders, including depression, cognitive decline, anxiety and stress.

Yeast based spreads (YBS) have long been a staple in many European, New Zealand and Australian households. The health benefits of such spreads, which include vegemite, marmite and prometite have long been promoted in familiar advertising campaigns such as “Happy little vegemites”, “my mate marmite”. However the discovery of the B vitamins in the early 1900s together with the associated health benefits resulted in these spreads being included amongst the soldier’s rations during the first world war. Despite this, there are limited studies available on the effects of YBS and health outcomes. Recently, YBS were used as a complete nutrient source for yeast to efficiently grow and ferment in low level glucose solutions, effectively creating “vegemite beer” (Kerr & Schulz, 2016). In addition, people who consume a daily teaspoon of marmite, showed modulated cortical excitation and inhibition, presumably due to increased levels of the inhibitory neurotransmitter gamma-aminobutyric acid, as an effect to the high levels of vitamin B12 in marmite, hence, marmite may help regulate brain function (Smith, Wade, Penkman, & Baker, 2017)

Although much research has been done on dietary vitamin B supplementation and sources, there may be a role for researching vegemite, marmite, promite and other such YBS as they are products common to most supermarket shelves. YBS traditionally were made from the leftover products of brewer's yeast as a by-product of beer brewing. There is paucity of data available highlighting the nutritional benefits of including YBS in the diet. These spreads are some of the richest known foods containing B vitamins. Notably, vitamin B12 is not naturally found in these spreads and added into some brands during manufacturing.

The aim of this study was to assess whether people who consumed YBS, scored showed better mood and stress levels than those people who did not consume YBS. The premise behind the study, was that YBS are high in B vitamins and that people who consume B vitamins regularly will not suffer from B vitamin deficiencies which can be a contributing factor to poor mental health. YBS are a cheap and accessible option for people looking to increase their intake of vitamin B and could be prove to be a valuable addition to the everyday diet and a significant prescriptive dosage of vitamin B. It was hypothesized that individuals consuming YBS would have better levels of depressive, anxiety and stress symptoms than people who did not consume these spreads, even after adjusting for covariates. Further, it was hypothesized that B12 enriched spreads would infer the greatest benefit above and beyond that from other YBSs.

2. Methods

2.1. Survey Development

The survey was designed to determine the effect of consumption of YBS on levels of depression anxiety and stress in the community. Ethics was approved by the Victoria University human research ethics committee (HRE15-159) in July 2015. Other secondary questions included gender, age, geography, medical condition, previous or current history of depression or anxiety, diet choice, soy milk consumption, dose of YBS consumption and how often and vitamin supplementation.

2.2. Survey general questions

Questions on YBS consumption was important to determine what type of B vitamins were consumed and at what dosage they were being consumed at. Not all YBS have the same vitamin B content. For example, vegemite original, ozemite and vege-spread contain vitamin B1, B2, B3 and B9 (Table 1). Promite contains vitamin B1, B2 and B3 whilst marmite, ausiemite and mightymite contain vitamin B1, B2, B3, B9 and B12 and vegemite salt reduced (available as of December 2014) contains B1, B2, B3, B6, B9, B12 (Table 1). Participants were asked about diet choices so that the researchers could assess the impact of diet choices on B vitamin intake and account for this in the analysis. Questions relating to past mental health helped ascertain the psychological profile of the respondents and any mitigating factors that may cause them to be more susceptible to anxiety and stress. All authors had full access to all the data (including statistical reports and tables) in this study.

2.3. Depression, Anxiety, Stress Scale

The depression, anxiety, stress scale (DASS) was chosen to be embedded in the questionnaire for several reasons. It was scale appropriate for clinical and non-clinical samples and provides a measure of stress which inclines to be more sub-syndromal than depression or anxiety. This scale can be used for both research and clinical purposes and was developed in Australia. This scale is much longer and includes 42 questions and is intended to take between 5-10 minutes to complete. Each question is rated on a 4-point Likert scale to determine frequency and severity of the survey subjects within the last week. Answers ranged from 'did not apply to me at all', to 'applied to me very much', or 'most of the time'. The DASS42 has strong construct validity (Crawford & Henry, 2003) as well as adequate discriminant and convergent validity (Lovibond & Lovibond, 1995). DASS has adequate internal consistency, with reported Cronbach's alpha coefficients of 0.71, 0.79 and 0.81 respectively (Brown, Chorpita, Korotitsch, & Barlow, 1997). When scoring DASS, patients with a higher score are perceived to be experiencing greater depression, anxiety and stress than those with a lower score. The format of the questions in DASS are suitable for inclusion into a questionnaire survey format and the scale is fully validated (Lovibond & Lovibond, 1995). The primary endpoint of the DASS42 is to determine degree

and severity in emotional disturbances of depression, anxiety and stress. A score is given which is categorized in 5 different ranges, normal, mild, moderate, severe, extremely severe.

2.4. The yeast based spread survey

2.4.1. Subjects

All participants were recruited online. The survey was distributed via social media including twitter and facebook via sites referring to health, nutrition and mental issues etc. Participants were also recruited by advertisement around Victoria University as well as in cafes, hospitals and around the community. In addition, the survey was included in electronic emails that were sent to 6,000 business owners around Melbourne, VIC Australia (e-west, e-east, e-south, e-north). Inclusion criteria included individuals who self-nominated to undertake the online survey. Exclusion criteria included those who were less than 18 years of age. The procedure that was used was in the format of a survey.

2.4.2. Measures

Outcome measures in the present YBS survey include levels of general psychological distress, depression, and anxiety and general health. Symptoms of depression, anxiety, and stress were assessed using the short form of DASS42 (Lovibond & Lovibond, 1995) embedded within the YBS survey. Participants were asked to answer questions concerning their age, marital status, gender, number of dependents as well as all questions as stated in 2.1.1. In total, the survey consisted of 71-questions.

The information to participant's form was embedded as the first question of the survey. The second question of the survey consisted of the patient consent form, and by clicking "yes" it progressed the participant to question 3, the first question relating to the YBS-questionnaire. The Survey was launched on the Victoria University Qualtrics site on 24 August 2015 and remained until 28 November 2016.

2.4.3. Statistical Analysis

Data were analysed using SPSS version 23. Data were screened for normality (inspecting skewness and kurtosis). All results for depression, anxiety and stress scales fell within normal ranges so data throughout were analysed using parametric statistics. ANCOVA's were utilized to assess the impact of yeast based spread consumption and a range of covariates on the depression, anxiety and stress scales. Post-hoc tests (where appropriate) utilized the data from the simple main effects analysis with the application of a Bonferroni correction to adjust for experiment-wise error rates. Analysis of both stress ANCOVA's showed that Levene's test of homogeneity was violated. These data were further screened through calculation of variance ratios which indicated the data were suitable for parametric analyses as ratios were 1.38 (when contrasting people who ate and did not eat YBSs) and 1.67 (contrasting YBS eaters, B12 enriched YBS eaters and controls), well below threshold for homogeneity (see Fields, 2005). Finally, analysis of dose response relationships between consuming yeast based spreads and significant mood subscales as well as the consumption of B12 enriched yeast based spreads and these scales were conducted using a Pearson's Product Correlation Coefficient (PPMCC).

3. Results

3.1. Patient demographics

The final sample size of 520 participants was derived from a total of 678 surveys begun by participants. Of the 158 excluded surveys, 133 were incomplete (i.e. did not commence the DASS) or did not progress past the consent question, 22 were excluded as incomplete duplicates or with missing values and 3 were excluded as statistical outliers (>2 standard deviations from the mean) across all 3 DASS measures. Demographic variables for the cohort are reported in Table 2 according to medical, dietary and supplement characteristics.

3.2. Yeast based spread consumption improves anxiety and stress scores but not depression.

A one-way ANCOVA was used to determine whether there was a statistically significant difference between people who did and did not consume YBS on depressive symptoms whilst controlling for gender, what type of diet the person usually ate, what supplements they consumed, consumption of soy milk, consumption of alcohol and a history of depression or anxiety as covariates. The results of the analysis indicated no significant effect of yeast based spread consumption on depression scores between groups, $F(1, 511) = 2.263$, $p=0.133$, $\eta^2=0.04$ and $power\ 0.324$ (Figure 1).

A similar one-way ANCOVA was used to determine differences in anxiety levels between people who did and did not consume YBS. This ANCOVA (and all following utilized the same covariates as above). The results of this ANCOVA revealed a significant impact of eating YBS on anxiety, $F(1,511) = 5.908$, $p=0.015$, $\eta^2=0.012$, $power=0.679$. Two covariates also demonstrated a (controlled for) effect on anxiety, soy milk consumption and previous depressive history (Figure 1).

Finally, an ANCOVA was utilized to assess the impact of consuming yeast based spread consumption on subjective levels of stress in the context of covariates. The results of this analysis indicated a significant effect of YBS, $F(1,511) = 8.358$, $p=0.004$, $\eta^2=0.016$, $power=0.823$. The same two factors showed significant (controlled for) effects, namely consumption of soy milk and previous diagnosis of depression or anxiety. Figure 1 highlights the results of the depression, anxiety and stress analysis for the consumption of YBS or not.

A PPMCC (Pearson Correlation co-efficient) of the anxiety and stress scales of the DASS indicated no significant dose response effect of eating different amounts of yeast based spreads on these factors (i.e. greater consumption per month was not related to variation in improved scores). More specifically, there was no significant correlation between amount consumed per month and anxiety level, $r(325) = 0.038$ $p=0.492$, or stress levels $r(325)=0.032$, $p=0.561$.

3.3. Vitamin B12 fortification in yeast based spreads improve stress scores

A further three ANCOVA's were conducted to investigate group differences between those who do not consume YBS, those who consume non-fortified YBS (i.e. no B12) and those who consume B12 fortified YBS. The results of the ANCOVAs indicated no significant differences on depression ($F(2, 510) = 1.105, p = 0.332, \eta^2 = 0.004, power = 0.244$) or anxiety ($F(2, 510) = 2.749, p = 0.065, \eta^2 = 0.011, power = 0.524$) when participants were broken down into the three groups. In contrast, assessing the stress dimension of the DASS indicated a significant difference between groups, $F(2, 510) = 5.177, p = 0.006, \eta^2 = 0.020, power = 0.827$. Simple main effects analysis of these differences indicated they existed between the B12 fortified yeast based spread consuming group and the no yeast based spread group. These results are highlighted in (Figure 2.) Notably, the stress analysis again highlighted soy milk consumption and history of depressive or anxiety disorder as significant covariates that were controlled.

Finally, a PPMCC was used to determine any dose response relationship between amount of B12 enriched yeast based spread consumed per month and the significant variable of stress as depicted in (Figure 2.) The results of the correlation analysis indicated no significant correlation between quantity and stress levels, $r(105) = -0.140, p = 0.151$.

4. Discussion

This study assessed whether the consumption of YBS have the potential to improve mental health in a community sample via a nationwide survey. It was hypothesized that the consumption of YBS might be associated with lower reporting of depression, anxiety and stress symptoms than those who do not consume YBS. The results indicate that people who consume YBS regularly show significantly less anxiety and stress (but not depression) compared to those who do not consume YBS. In addition, the results supported the hypothesis that those who consume YBS fortified with B12 would show better stress scores (but not anxiety and depression) on the DASS42 scale than those who do not.

4.1. Vitamin B deficiency in depression, anxiety and stress

Vitamin B1, B2, B3, B6, B9 and B12 have been implicated as protective risk factors against depression, anxiety and stress. Vitamin B are known to lower homocysteine levels and preserve brain function. There are established relations between deficiency in vitamin B1, B2, B3, B6, B9 and B12 (all or each individually or combinations thereof) and depression, anxiety and stress (Mikkelsen, Stojanovska, & Apostolopoulos, 2016; Mikkelsen, Stojanovska, Prakash, & Apostolopoulos, 2017; Mikkelsen, Stojanovska, Tangalakis, Bosevski, & Apostolopoulos, 2016).

Vitamin B1 (thiamine) deficiency has detrimental neurological effects. (Abdou & Hazell, 2014; Combs, 2008; Zhang et al., 2013). Vitamin B2 (riboflavin) deficiency primarily results in anaemia, inflammation, depression, migraines, and affects cognitive function. (Massey, 2000; Murakami et al., 2008; Pinto & Cooper, 2014; Powers, 2003). Vitamin B3 (niacin) deficiency results in Pellagra, known for its symptoms of, insomnia, mental confusion, psychosensory disturbances, psychomotor disturbances, emotional disturbances, anxiety, depression and hallucinations. It is believed that lack of vitamin B3 and other B vitamins in processed food diets can be attributed to a rise in mental health disorders and violent crimes in recent decades (Fu, Doreswamy, & Prakash, 2014; Kamanna, Ganji, & Kashyap, 2009; Li et al., 2010; Prakash, Gandotra, Singh, Das, & Lakra, 2008; Smesny, Baur, Rudolph, Nenadic, & Sauer, 2010; Thompson & Proctor, 1953).

Low levels of B9 is often seen in the plasma of people suffering from depression (Loria-Kohen et al., 2013; M. Malouf, Grimley, & Areosa, 2003; Mitchell, Conus, & Kaput, 2014; Murakami et al., 2008; Nilsson, Gustafson, & Hultberg, 2001; Obeid & Herrmann, 2006; Pan et al., 2012; Pitkin, 2007) and a number of studies suggest that the status of vitamin B9 plays a major role in depression, as vitamin B9 is a vital precursor for the formation of neurotransmitters such as serotonin, epinephrine, nicotinamides, purines and phospholipids. A deficiency in vitamins B6 and B12 has been attributed to severe symptoms of depression and cognitive decline. Indeed, vitamin B12 deficiency is found in up to one-third of depressed patients and increased vitamin B12 levels are associated with improved treatment outcomes of patients with depression. In addition, B12 deficiency increases the risk of cognitive decline (Balk et al., 2007; Bell et al., 1991; Bell et al., 1992; Carney, Williams, & Sheffield, 1979; Holsboen, Benkert, Meier, & Kreuz-Kersting, 1985; Sengul et al., 2014). Many B vitamins act as co-enzymes in enzymatic reactions as specific

carriers of functional groups. As a group, they participate in the metabolism of carbohydrate, protein, lipids, vitamins, minerals and drugs whilst taking part in many other cellular metabolic functions including DNA synthesis (Hvas, Juul, Bech, & Nexø, 2004; R. Malouf & Grimley Evans, 2003; Martin, Singleton, & Hiller-Sturmhofel, 2003; Miller, 2008).

Given the high dosage of B vitamins within YBS, we attribute this lowering of DAS scores effect to the consumption of higher doses of vitamin B within the diet. However, we cannot unequivocally assume that the vitamin B is causing this effect alone. YBS are often consumed in the morning spread on toast or bread (although the survey did not specify which meal the YBS was mostly eaten). There may be a correlation between lower DASS scores and breakfast consumption. In 2013, the Korean community health survey investigated the association between the frequency of eating breakfast and depression in adults. The survey covered a 20-year span and recruited 207, 710 participants. Participants were grouped into the categories, regarding breakfast consumption as “Seldom”, “sometimes” and “always”. Results of the survey indicated that participants who had breakfast “seldom” or “sometimes” had significantly higher depressive symptoms than those who “always” had breakfast. A possible weakness in this study lies in that “depressive symptoms” was measured using the Korean community health survey question by only one question “Have you experienced sorrowful or despairing emotions affecting your daily life more than two weeks over the past year?”

Yeast based spreads contain high quantities of vitamin B plus high quantities of amino acids such as tryptophan which is a precursor for the neurotransmitter serotonin. Many studies have used a technique of acute tryptophan depletion to observe the effect of lowered serotonin levels in the human brain (Young, 2013) Serotonin acts in the body as a natural mood stabilizer and decreases in serotonergic neurotransmitter tone have been associated with low mood and depression. As marmite has 144 mg of tryptophan (Government, 2017) it may be prudent to investigate to what end the presence of tryptophan in the YBS has on the lowering of DASS scores.

The limitations of this study include the uncertainty that the lowered DASS scores are a by-product of vitamin B intake or some other component of the YBS, or even a synergistic effect of all the components of YBS.

4.2. Vitamin B supplementation and the effect on stress

Previous studies have shown that micronutrient supplementation, in particular B vitamins, has a beneficial effect on improving mood states, perceived stress, and mild psychiatric symptoms, outwardly healthy individuals (Long & Benton, 2013) Indeed, in a double blind randomized control study the effects of Berocca (a multivitamin and mineral supplement with high levels of vitamin B) on psychological status, indicated that Berocca significantly lowered levels of anxiety and perceived stress in 80 healthy male volunteers (Carroll, Ring, Suter, & Willemsen, 2000). In addition, the effect of Blackmores Executive B Stress Formula over six months' duration on work place stress and mood showed that subjects that took the Executive B formula after 12 weeks reported significantly lower personal strain and a reduction in confusion and depressed/dejected mood (Stough et al., 2011). Furthermore, a multiple-dose, double-blind, placebo- controlled, double-centre study with 300 patients for 30 days assessed the effects of a multivitamin combination (Berocca, calcium, magnesium) on stress on a large cohort of South Africans. It was shown that there were statistically significant improvements in all psychometric tests in those that took the Berocca, calcium, magnesium combination compared to the placebo group. Our study is the first to assess the link between depression anxiety and stress and micro nutrient supplementation in the form of YBS.

4.3. The role of vitamin B9 and B12 on stress

Depressive episodes are well known to occur after a major negative life event and that often the stresses related to these events are causal for the onset of depression. Stress responses are an adaptive process used by the body to maintain homeostasis and act, under threat, however prolonged stress responses triggered by the everyday stressors of

work, family, finances and relationships can be damaging to health and lead to disease and depression (Schneiderman, Ironson, & Siegel, 2005).

Vitamin B12 together with B9 and B6 are 3 of the key vitamins that have direct effect on mood and neurotransmitter regulation. The functions of all however are intricately linked as they play complimentary roles within the folate and methionine cycles in which methionine synthetase catalyzes the methylation of homocysteine into methionine. If this methylation process does not occur efficiently, high levels begin to build up in the blood. Based on epidemiological and longitudinal data, elevated serum homocysteine levels is a predictive risk factor for cognitive impairment and other neurological disorders (Sachdev, 2005). In fact meta-analysis studies in which 17 trials, involving 39,107 participants and 12 trials involving 47,429 participants noted that homocysteine levels were reduced with a steady administration of folic acid \pm vitamins B12 and B6 (Marti-Carvajal, Sola, & Lathyris, 2015; Mei, Rong, Jinming, Yongjun, & Hui, 2010) Results from our study have shown that YBS fortified with vitamin B12 contributes to reducing stress and anxiety in consumers. It is interesting to note however, that all spreads which contained vitamin B12 fortification also contained vitamin B9. It may be interesting to investigate whether the lowering of DAS scores is attributed alone to the fortification with B12 or the synergistic combination of B12 and B9.

4.4. Conclusion

We demonstrated that the survey participants who indicate that they consume YBS score lower in the anxiety and stress subscales of the DASS than do participants who do not eat YBS. Furthermore, those who consume YBS with added B12 score lower on stress on the DASS scale than those who consume yeast based spreads without B12. There was no evidence to suggest that dosage had any effect on DASS scores. There may be great benefit to the community in finding an easily accessible vitamin B source which when taken regularly can augment nutritional dietary intake of vitamin B to therapeutic levels. There are numerous groups within the community that could benefit from and cheap, easily accessible form of vitamin B. These include hospitalised patients with decreased appetites, children who are fussy eaters, vegetarians, vegans, elderly people, low income families and people suffering from drug and alcohol addiction who may be nutritionally depleted.

The positive results generated by this survey on YBS and DASS scores indicate that regular consumption of YBS lowers anxiety and stress scores, and those consuming YBS with added vitamin B12 have further improvements in stress scores. Thus, regular consumption of YBS may help to lower the incidence of anxiety and stress in the community. Further studies will need to be undertaken in order to strengthen the data gathered so far providing a link between YBS consumption and decreasing levels of depression anxiety and stress.

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Competing interests

The authors have declared no conflict of interest.

References

- Abdou, E., & Hazell, A. S. (2014). Thiamine Deficiency: An Update of Pathophysiologic Mechanisms and Future Therapeutic Considerations. *Neurochem Res*. doi: 10.1007/s11064-014-1430-z
- Balk, E. M., Raman, G., Tatsioni, A., Chung, M., Lau, J., & Rosenberg, I. H. (2007). Vitamin B6, B12, and folic acid supplementation and cognitive function: a systematic review of randomized trials. *Arch Intern Med*, 167(1), 21-30. doi: 10.1001/archinte.167.1.21
- Bell, I. R., Edman, J. S., Morrow, F. D., Marby, D. W., Mirages, S., Perrone, G., . . . Cole, J. O. (1991). B complex vitamin patterns in geriatric and young adult inpatients with major depression. *J Am Geriatr Soc*, 39(3), 252-257.
- Bell, I. R., Edman, J. S., Morrow, F. D., Marby, D. W., Perrone, G., Kayne, H. L., . . . Cole, J. O. (1992). Brief communication. Vitamin B1, B2, and B6 augmentation of tricyclic

- antidepressant treatment in geriatric depression with cognitive dysfunction. *J Am Coll Nutr*, 11(2), 159-163.
- Beyondblue. (2014). Beyond Blue- Depression and Anxiety . (<http://www.beyondblue.org.au>). .
- Brown, T. A., Chorpita, B. F., Korotitsch, W., & Barlow, D. H. (1997). Psychometric properties of the Depression Anxiety Stress Scales (DASS) in clinical samples. *Behav Res Ther*, 35(1), 79-89.
- Burns, J., & Birrell, E. (2014). Enhancing early engagement with mental health services by young people. *Psychol Res Behav Manag*, 7, 303-312. doi: 10.2147/PRBM.S49151
- Carney, M. W., Williams, D. G., & Sheffield, B. F. (1979). Thiamine and pyridoxine lack newly-admitted psychiatric patients. *Br J Psychiatry*, 135, 249-254.
- Carroll, D., Ring, C., Suter, M., & Willemsen, G. (2000). The effects of an oral multivitamin combination with calcium, magnesium, and zinc on psychological well-being in

- healthy young male volunteers: a double-blind placebo-controlled trial. *Psychopharmacology (Berl)*, 150(2), 220-225.
- Combs, G. F. (2008). *The Vitamins: Fundamental Aspects in Nutrition and Health* San Diego Elsevier.
- Craske, M. G., Rauch, S. L., Ursano, R., Prenoveau, J., Pine, D. S., & Zinbarg, R. E. (2009). What is an anxiety disorder? *Depress Anxiety*, 26(12), 1066-1085. doi: 10.1002/da.20633
- Crawford, J. R., & Henry, J. D. (2003). The Depression Anxiety Stress Scales (DASS): normative data and latent structure in a large non-clinical sample. *Br J Clin Psychol*, 42(Pt 2), 111-131. doi: 10.1348/014466503321903544
- Dale, E., Bang-Andersen, B., & Sanchez, C. (2015). Emerging mechanisms and treatments for depression beyond SSRIs and SNRIs. *Biochem Pharmacol*, 95(2), 81-97. doi: 10.1016/j.bcp.2015.03.011
- Fu, L., Doreswamy, V., & Prakash, R. (2014). The biochemical pathways of central nervous system neural degeneration in niacin deficiency. *Neural Regen Res*, 9(16), 1509-1513. doi: 10.4103/1673-5374.139475
- Government, V. S. (2017). Spread, yeast, marmite. *Home - Healthy living - Food profiles*
Retrieved 12th june 2017, from https://http://www.betterhealth.vic.gov.au/health/foodprofiles/Spread_yeast_marmite
- Holsboen, F., Benkert, O., Meier, L., & Kreuz-Kersting, A. (1985). Combined estradiol and vitamin B6 treatment in women with major depression. *Am J Psychiatry*, 142(5), 658.
- Hvas, A. M., Juul, S., Bech, P., & Nexø, E. (2004). Vitamin B6 level is associated with symptoms of depression. *Psychother Psychosom*, 73(6), 340-343. doi: 10.1159/000080386
- Kamanna, V. S., Ganji, S. H., & Kashyap, M. L. (2009). The mechanism and mitigation of niacin-induced flushing. *Int J Clin Pract*, 63(9), 1369-1377. doi: 10.1111/j.1742-1241.2009.02099.x
- Kerr, E. D., & Schulz, B. L. (2016). Vegemite Beer: yeast extract spreads as nutrient supplements to promote fermentation. *PeerJ*, 4, e2271. doi: 10.7717/peerj.2271
- Li, D., Sun, W. P., Zhou, Y. M., Liu, Q. G., Zhou, S. S., Luo, N., . . . Guo, M. (2010). Chronic niacin overload may be involved in the increased prevalence of obesity in US children. *World J Gastroenterol*, 16(19), 2378-2387.
- Long, S. J., & Benton, D. (2013). Effects of vitamin and mineral supplementation on stress, mild psychiatric symptoms, and mood in nonclinical samples: a meta-analysis. *Psychosom Med*, 75(2), 144-153. doi: 10.1097/PSY.0b013e31827d5fbd
- Loria-Kohen, V., Gomez-Candela, C., Palma-Milla, S., Amador-Sastre, B., Hernanz, A., & Bermejo, L. M. (2013). A pilot study of folic acid supplementation for improving

- homocysteine levels, cognitive and depressive status in eating disorders. *Nutr Hosp*, 28(3), 807-815. doi: 10.3305/nh.2013.28.3.6335
- Lovibond, P. F., & Lovibond, S. H. (1995). The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behav Res Ther*, 33(3), 335-343.
- Malouf, M., Grimley, E. J., & Areosa, S. A. (2003). Folic acid with or without vitamin B12 for cognition and dementia. *Cochrane Database Syst Rev*(4), CD004514. doi: 10.1002/14651858.CD004514
- Malouf, R., & Grimley Evans, J. (2003). The effect of vitamin B6 on cognition. *Cochrane Database Syst Rev*(4), CD004393. doi: 10.1002/14651858.CD004393
- Mann, J. J. (1999). Role of the serotonergic system in the pathogenesis of major depression and suicidal behavior. *Neuropsychopharmacology*, 21(2 Suppl), 99S-105S. doi: 10.1016/S0893-133X(99)00040-8
- Marti-Carvajal, A. J., Sola, I., & Lathyris, D. (2015). Homocysteine-lowering interventions for preventing cardiovascular events. *Cochrane Database Syst Rev*, 1, CD006612. doi: 10.1002/14651858.CD006612.pub4
- Martin, P. R., Singleton, C. K., & Hiller-Sturmhofel, S. (2003). The role of thiamine deficiency in alcoholic brain disease. *Alcohol Res Health*, 27(2), 134-142.
- Massey, V. (2000). The chemical and biological versatility of riboflavin. *Biochem Soc Trans*, 28(4), 283-296.
- Mei, W., Rong, Y., Jinming, L., Yongjun, L., & Hui, Z. (2010). Effect of homocysteine interventions on the risk of cardiocerebrovascular events: a meta-analysis of randomised controlled trials. *Int J Clin Pract*, 64(2), 208-215. doi: 10.1111/j.1742-1241.2009.02207.x
- Meldrum, B. S. (2000). Glutamate as a neurotransmitter in the brain: review of physiology and pathology. *J Nutr*, 130(4S Suppl), 1007S-1015S.
- Mikkelsen, K., Stojanovska, L., & Apostolopoulos, V. (2016). The Effects of Vitamin B in Depression. *Curr Med Chem*, 23(38), 4317-4337.
- Mikkelsen, K., Stojanovska, L., Prakash, M., & Apostolopoulos, V. (2017). The effects of vitamin B on the immune/cytokine network and their involvement in depression. *Maturitas*, 96, 58-71. doi: 10.1016/j.maturitas.2016.11.012
- Mikkelsen, K., Stojanovska, L., Tangalakis, K., Bosevski, M., & Apostolopoulos, V. (2016). Cognitive decline: A vitamin B perspective. *Maturitas*, 93, 108-113. doi: 10.1016/j.maturitas.2016.08.001
- Miller, A. L. (2008). The methylation, neurotransmitter, and antioxidant connections between folate and depression. *Altern Med Rev*, 13(3), 216-226.
- Mitchell, E. S., Conus, N., & Kaput, J. (2014). B vitamin polymorphisms and behavior: Evidence of associations with neurodevelopment, depression, schizophrenia, bipolar disorder and cognitive decline. *Neurosci Biobehav Rev*, 47C, 307-320. doi: 10.1016/j.neubiorev.2014.08.006
- Murakami, K., Mizoue, T., Sasaki, S., Ohta, M., Sato, M., Matsushita, Y., & Mishima, N. (2008). Dietary intake of folate, other B vitamins, and omega-3 polyunsaturated fatty acids

- in relation to depressive symptoms in Japanese adults. *Nutrition*, 24(2), 140-147. doi: 10.1016/j.nut.2007.10.013
- Murray, C. J., & Lopez, A. D. (1997). Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. *Lancet*, 349(9063), 1436-1442. doi: 10.1016/S0140-6736(96)07495-8
- Niciu, M. J., Kelmendi, B., & Sanacora, G. (2012). Overview of glutamatergic neurotransmission in the nervous system. *Pharmacol Biochem Behav*, 100(4), 656-664. doi: 10.1016/j.pbb.2011.08.008
- Nilsson, K., Gustafson, L., & Hultberg, B. (2001). Improvement of cognitive functions after cobalamin/folate supplementation in elderly patients with dementia and elevated plasma homocysteine. *Int J Geriatr Psychiatry*, 16(6), 609-614.
- Obeid, R., & Herrmann, W. (2006). Mechanisms of homocysteine neurotoxicity in neurodegenerative diseases with special reference to dementia. *FEBS Lett*, 580(13), 2994-3005. doi: 10.1016/j.febslet.2006.04.088
- Pan, W. H., Chang, Y. P., Yeh, W. T., Guei, Y. S., Lin, B. F., Wei, I. L., . . . Chen, W. J. (2012). Co-occurrence of anemia, marginal vitamin B6, and folate status and depressive

- symptoms in older adults. *J Geriatr Psychiatry Neurol*, 25(3), 170-178. doi: 10.1177/0891988712458365
- Pinto, J. T., & Cooper, A. J. (2014). From cholesterologenesis to steroidogenesis: role of riboflavin and flavoenzymes in the biosynthesis of vitamin D. *Adv Nutr*, 5(2), 144-163. doi: 10.3945/an.113.005181
- Pitkin, R. M. (2007). Folate and neural tube defects. *Am J Clin Nutr*, 85(1), 285S-288S.
- Powers, H. J. (2003). Riboflavin (vitamin B-2) and health. *Am J Clin Nutr*, 77(6), 1352-1360.
- Prakash, R., Gandotra, S., Singh, L. K., Das, B., & Lakra, A. (2008). Rapid resolution of delusional parasitosis in pellagra with niacin augmentation therapy. *Gen Hosp Psychiatry*, 30(6), 581-584. doi: 10.1016/j.genhosppsych.2008.04.011
- Ressler, K. J., & Nemeroff, C. B. (2000). Role of serotonergic and noradrenergic systems in the pathophysiology of depression and anxiety disorders. *Depress Anxiety*, 12 Suppl 1, 2-19. doi: 10.1002/1520-6394(2000)12:1+<2::AID-DA2>3.0.CO;2-4
- Sachdev, P. S. (2005). Homocysteine and brain atrophy. *Prog Neuropsychopharmacol Biol Psychiatry*, 29(7), 1152-1161. doi: 10.1016/j.pnpbp.2005.06.026
- Schneiderman, N., Ironson, G., & Siegel, S. D. (2005). Stress and health: psychological, behavioral, and biological determinants. *Annu Rev Clin Psychol*, 1, 607-628. doi: 10.1146/annurev.clinpsy.1.102803.144141
- Sengul, O., Uygur, D., Gulec, M., Dilbaz, B., Simsek, E. M., & Goktolga, U. (2014). The comparison of folate and vitamin B12 levels between depressive and nondepressive postmenopausal women. *Turk J Med Sci*, 44(4), 611-615.
- Smesny, S., Baur, K., Rudolph, N., Nenadic, I., & Sauer, H. (2010). Alterations of niacin skin sensitivity in recurrent unipolar depressive disorder. *J Affect Disord*, 124(3), 335-340. doi: 10.1016/j.jad.2009.12.017
- Smith, A. K., Wade, A. R., Penkman, K. E., & Baker, D. H. (2017). Dietary modulation of cortical excitation and inhibition. *J Psychopharmacol*, 31(5), 632-637. doi: 10.1177/0269881117699613
- Stough, C., Scholey, A., Lloyd, J., Spong, J., Myers, S., & Downey, L. A. (2011). The effect of 90 day administration of a high dose vitamin B-complex on work stress. *Hum Psychopharmacol*, 26(7), 470-476. doi: 10.1002/hup.1229
- Sullivan, G. M., Coplan, J. D., Kent, J. M., & Gorman, J. M. (1999). The noradrenergic system in pathological anxiety: a focus on panic with relevance to generalized anxiety and phobias. *Biol Psychiatry*, 46(9), 1205-1218.
- Thompson, L. J., & Proctor, R. C. (1953). Depressive and anxiety reactions treated with nicotinic acid and phenobarbital. *N C Med J*, 14(9), 420-426.
- van Stegeren, A. H. (2008). The role of the noradrenergic system in emotional memory. *Acta Psychol (Amst)*, 127(3), 532-541. doi: 10.1016/j.actpsy.2007.10.004
- Whitecloudfoundation. (2014). White cloud foundation - Depression Facts. (<http://www.whitecloudfoundation.org/depression-facts>). .
- Who press, G. S. (2008). The Global burden of disease: 2004 Update *World Health Organization*
- Yadid, G., & Friedman, A. (2008). Dynamics of the dopaminergic system as a key component to the understanding of depression. *Prog Brain Res*, 172, 265-286. doi: 10.1016/S0079-6123(08)00913-8
- Young, S. N. (2013). Acute tryptophan depletion in humans: a review of theoretical, practical and ethical aspects. *J Psychiatry Neurosci*, 38(5), 294-305. doi: 10.1503/jpn.120209

Zhang, G., Ding, H., Chen, H., Ye, X., Li, H., Lin, X., & Ke, Z. (2013). Thiamine nutritional status and depressive symptoms are inversely associated among older Chinese adults. *J Nutr*, 143(1), 53-58. doi: 10.3945/jn.112.167007

Table 1: Popular yeast based spreads and vitamin B content assessed in this study.

Yeast based spread brand (company)	B1	B2	B3	B6	B9	B12
Marmite (Sanitarium)	x	x	x		x	x
Vegemite original (Bega Cheese)	x	x	x		x	
Vegemite Salt Reduced (Bega Cheese)	x	x	x	x	x	x
Vegemite Cheesybite (Bega Cheese)	x	x	x	x	x	x
Vege spread (Freedom)	x	x	x		x	
Ozemite (Dick smith)	x	x	x		x	
MightyMite (Three threes)	x	x	x		x	x
AussieMite (AussieMite)	x	x	x		x	x
Promite (Master Foods)	x	x	x			

Table 2. Demographic, medical, dietary and supplement profile of sample

		Mean	N
Demographic and medical characteristics			
Gender	Male:Female		105:410
Age		44.9(13.6)	
Medical Condition	Diabetes		28
	Hypertension		67
	Elevated cholesterol		67
	Autoimmunity:cancer		30:10
	Other		49
Previous history of depression/anxiety	Yes:No		241:279
Dietary habits			
YBS Spread consumption	No		115
	No B12:B12 fortified		265:133
Duration of YBS consumption (years)		4.4(0.14)	
Diet choice	Omnivorous		415
	No red meat		22
	Paleo		16
	Vegetarian:Vegan		52:12
Soy Milk Consumption	No soy milk		404
	B12 fortified soy milk		100
	Non-fortified soy milk		14
Days per week soy milk consumers have soy milk		3.9(0.3)	
Number of standard alcoholic drinks per week		3.5(0.2)	
Number of alcohol drinking days per week		2.12(0.2)	
Supplement or medication use			
Supplement use (>= once per month)	Multivitamin		109
	Vitamin B		72
	Vitamin C		69
	Vitamin D		134
	Omega 3:Iron		102:47
	Vitamin B12		7
Currently taking antidepressant	Yes:No		49:472

Figure Legends

Fig. 1. Differences in DASS measure based on consumption of yeast based spreads (mean scores +/- standard error of the mean). * and ** denote significant differences between groups at the $\alpha=0.05$ and $\alpha=0.01$.

Fig. 2. Differences on DASS measure based on consumption of yeast based spreads with and without B12 fortification (mean scores +/- standard error of the mean). ** denotes significant differences between groups at the $\alpha=0.01$.

Figure 1

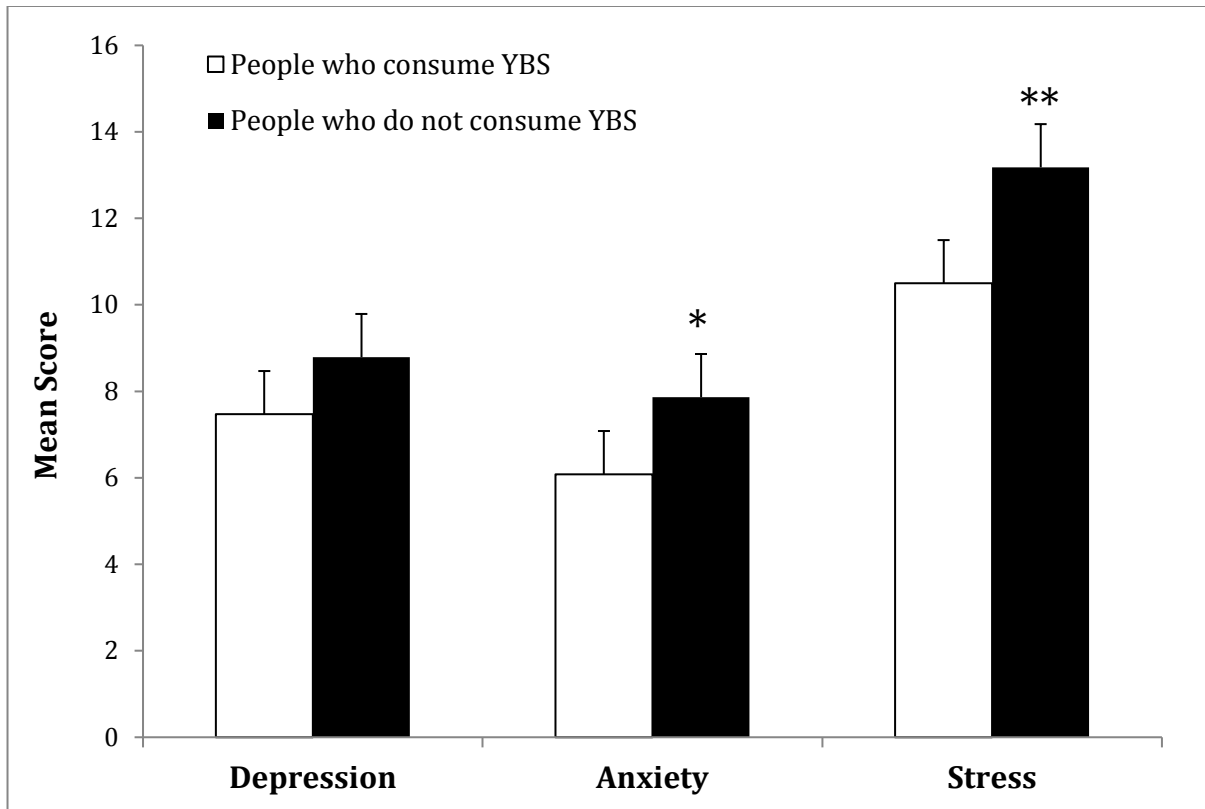


Figure 2

