The effect of multivitamin supplementation on mood and stress in healthy older men

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Objective There is a demonstrated association between poor mood and deficiency in several micronutrients. Multivitamin supplements contain a wide range of nutrients, suggesting that they may be effective in improving mood; however, few studies have investigated this potential in randomized, controlled trials. This study investigates the effects of a multivitamin, mineral, and herbal supplement on mood and stress in a group of healthy, older male volunteers.

Methods In this randomized, double-blind, placebo-controlled trial, fifty men, aged 50–69 years, supplemented for a period of 8 weeks with a multivitamin formulation that contained vitamins (at levels above recommended daily intakes), minerals, antioxidants, and herbal extracts, or a placebo. They completed a series of mood and stress questionnaires at baseline and post-supplementation.

Results Compared with placebo, there was a significant reduction in the overall score on a depression anxiety and stress scale and an improvement in alertness and general daily functioning in the multivitamin group.

Conclusions Supplementation with a multivitamin, mineral and herbal formulation may be useful in improving alertness and reducing negative mood symptoms and may also improve feelings of general day-to-day well-being. Copyright © 2011 John Wiley & Sons, Ltd.

key words— multivitamin supplementation; mood; depression; anxiety; stress; aging

INTRODUCTION

Poor mood has been associated with deficiency of a number of key micronutrients. For instance, there are associations between depressive symptoms and vitamin B12 and folic acid deficits, in that those individuals with lower levels of vitamin B12 and/or folic acid tend to have higher levels of depression or depressed mood (Alpert et al. 2000; Baldeiwicz et al. 2000; Tolmunen et al. 2003). Lower levels of vitamin D, zinc, selenium, and secondary changes in the concentrations of associated metabolites, such as methylmalonic acid and homocysteine, have also been associated with poorer mood, including anxiety and depression (Benton 2002; Levenson 2006; Wilkins et al. 2006; Stanger et al. 2009).

Vitamins and minerals such as these are commonly found together in multivitamin formulas, suggesting that multivitamin supplementation may be able to improve mood. However, the results of studies examining the effects of supplementation have been contentious. Although some have found no changes in mood after supplementation (Cockle et al. 2000; Hvas, Juul et al. 2004), or attributed improvements to a placebo effect (America and Milling 2008), others have found that supplementing with B-complex vitamins or multivitamins can improve mood or reduce depressive symptoms (Carroll et al. 2000; Gariballa and Forster, 2007a, 2007b). However, research in this area is limited.

Nevertheless, nutritional interventions and vitamin/mineral supplementations are among the most popular form of complementary therapies for the treatment of depression (Williams et al. 2005). Dietary supplements including vitamins, minerals, and herbal extracts...
are also used to treat anxiety, insomnia, and fatigue (Eisenberg et al. 1993; Eisenberg et al. 1998; Kessler et al. 2001). On the whole, the use of complementary and alternative therapies is increasing in Australia (MacLennan and Wilson 1996; MacLennan et al. 2002) and other developed countries, (Eisenberg et al. 1998; Kessler et al. 2001) and multivitamin supplementation is particularly popular (Kelly et al. 2005). With an increasing number of people opting to supplement, and given claims about supposed benefits of such supplements, more research is needed to support these marketing claims that are promoted to consumers.

Establishing the nature of the relationship between mood and nutritional supplementation may be particularly relevant for older people. Although older adults are less likely to report disorders such as clinical depression and anxiety, they more frequently suffer from milder, subclinical depressive conditions that are associated with significant impairment to quality of life (Kessler et al. 1997; Chachamovich et al. 2008). Also, elderly people in the general population who take vitamin supplements may not be clinically depressed, but may supplement in order to reduce or prevent mild depressive symptoms or to enhance general well-being and increase vitality (America and Milling 2008).

The majority of research to date investigating the use of multivitamin supplementation on mood symptoms has been done so in clinical populations rather than in healthy adults. One recent exception is a study reporting improved mood following a 33-day intervention of high-dose B-complex vitamin in a cohort of healthy men aged from 30 to 55 years (Kennedy et al. 2010). This study demonstrated that vitamin supplementation is capable of improving mood in psychologically intact younger adults. The current study extends these findings, using similar assessments of subjective mood (Profile of Mood States, Visual Analog Scales), perceived stress (Perceived Stress Scale), and psychological health (General Health Questionnaire) assessing the mood effects of a multivitamin supplement in an older population (50 to 69 years old) who may benefit more from such an intervention. Given the prevalence of subclinical depressive symptomatology in this population, the current study also included a validated measure of these symptoms (the Depression, Anxiety, and Stress Scale). In order to better capture the long-term effects of supplementation, this study also employed a longer intervention treatment of 8 weeks.

The aim of the current study was, therefore, to assess the role of a commonly used multivitamin supplement containing vitamins, minerals, antioxidants, and herbs on mood and stress variables in a group of healthy older male volunteers. It was hypothesized that supplementation with multivitamins would improve clinical mood symptoms, subjective mood experience, and stress, above that of placebo.

METHODS

Design

The study followed a double blind, randomized, placebo controlled, parallel groups design. Testing was conducted prior to (Baseline) and then following 8 weeks supplementation (Post-treatment) with either a multivitamin or placebo.

Participants

Male participants in the age range of 50–69 years were recruited by way of newspaper advertisements, posters, and e-mails. The participants were initially screened by telephone. Exclusion criteria included a history of head injury, diabetes, heart disease, nutritional or herbal allergy or intolerance, neurological, psychological or psychiatric disorder, alcohol or drug dependency, and the current use of blood thinning medication. The participants were in a sedentary occupation or did little exercise, were non-smokers, and were not presently supplementing with multivitamins or similar products. At the first session, they were screened using the Mini Mental State Questionnaire (MMSE; Folstein et al. 1975). A score of 27/30 or greater was chosen as the cutoff. All the participants gave written informed consent. The study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the Swinburne University Human Research Ethics Committee.

Fifty-six participants were enrolled in the study. Of these, five did not return for post-supplementation testing and one was excluded due to additional vitamin supplementation during the study. Therefore, 50 participants completed the study and were used in the analysis. For some measures, individual data were incomplete or illegible. In addition, four of the Depression Anxiety Stress Scale (DASS) and five of the General Health Questionnaire (GHQ), respectively, were incomplete.

Supplements

The multivitamin used in the current study was Swiss Men’s Ultivite®, a formulation which is widely available in Australia and contains vitamins at levels exceeding recommended daily intakes, as well as minerals, herbs, and antioxidants. The vitamins and minerals contained in the supplement are listed in Table 1. A combination of 21 herbal, fruit, and vegetable extracts were included at levels ranging from 10 mg to 200 mg (dry or fresh plant equivalent). These included ginseng,
ginkgo, parsley, ginger, fennel, gotu kola, papaya, barberry, and tomato. A full list can be obtained from the corresponding author. The placebo tablets looked identical to the multivitamin preparation and contained starch and a small amount of riboflavin (2 mg) to give them a similar smell and coloration of the urine. Treatment preparation was performed by Swisse Vitamins Pty Ltd (Collingwood, Victoria Australia) who provided the multivitamin and placebo tablets in identical, randomized, numbered bottles and held the blinding codes until completion of the study.

Health and mood assessments

The following assessment instruments were administered to the participants in randomized order, with the same pre-treatment and post-treatment order for each participant. These instruments were chosen for the current study as they assess a number of aspects of mood including subjective mood experience, perceived stress, generalized mood, and general health, as well as clinical mood disturbance. Furthermore, the questionnaires address different time scales allowing for a broader picture of the individual’s mood state. The suite of questionnaires took approximately 60 min to complete. Assessment took place at baseline and at the end of supplementation.

General Health Questionnaire (Goldberg 1978)

The GHQ comprises 60 items and assesses changes in the ability to carry out normal daily functions, or the appearance of new symptoms including somatic symptoms and insomnia, or feelings that may indicate psychological disorder such as anxious or depressed feelings (McDowell 2006). Responses are given on a 4-point scale ranging from 0 – “much less than usual” to 3 – “much more than usual” and relate to behavior “over the last few weeks”. The sum gives a score with a possible range of 0–180, with higher scores indicating more negative feelings or experiences.

The Depression Anxiety Stress Scale (Lovibond and Lovibond 1995)

This is a short questionnaire comprising three subscales: depression, anxiety, and stress. It is relevant for both clinical and non-clinical populations. The 21 items encompass a range of affect-related symptoms, including physical symptoms (e.g., dry mouth) and mood symptoms (e.g., agitation). Responses are made on a 4-point scale from 0 to 3, yielding a possible range from 0 to 63, with higher scores indicating more symptoms. A score of zero does not indicate positive mood, but rather a lack of symptoms associated with dysphoric mood. Questions pertain to feelings “over

Table 1. Vitamin and mineral composition of the multivitamin supplement and recommended daily intake (NHMRC 2005)

<table>
<thead>
<tr>
<th>Supplement</th>
<th>RDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin E (d-alpha-tocopheryl acid succinate)</td>
<td>41.33 mg</td>
</tr>
<tr>
<td>Vitamin B1 (thiamine hydrochloride)</td>
<td>30 mg</td>
</tr>
<tr>
<td>Vitamin B2 (riboflavin)</td>
<td>30 mg</td>
</tr>
<tr>
<td>Vitamin B3 (nicotinamide)</td>
<td>30 mg</td>
</tr>
<tr>
<td>Vitamin B5 (calcium pantothenate)</td>
<td>70 mg (equiv. Pantothenic Acid 64.13 mg)</td>
</tr>
<tr>
<td>Vitamin B6 (pyridoxine hydrochloride)</td>
<td>30 mg</td>
</tr>
<tr>
<td>Vitamin B12 (cyanocobalamin)</td>
<td>30 mcg</td>
</tr>
<tr>
<td>Biotin</td>
<td>50 mcg</td>
</tr>
<tr>
<td>Folic acid</td>
<td>500 mcg</td>
</tr>
<tr>
<td>Calcium ascorbate dihydrate</td>
<td>200 mg (equiv. Ascorbic acid (Vitamin C) 165.2 mg)</td>
</tr>
<tr>
<td>Choline bitartrate</td>
<td>25 mg</td>
</tr>
<tr>
<td>Inositol</td>
<td>25 mg</td>
</tr>
<tr>
<td>Bioflavonoids</td>
<td>40 mg</td>
</tr>
<tr>
<td>Lysine hydrochloride</td>
<td>50 mg</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>1 mg</td>
</tr>
<tr>
<td>Calcium citrate</td>
<td>100 mg (equiv. Calcium 21 mg)</td>
</tr>
<tr>
<td>Magnesium oxide – heavy</td>
<td>100 mg (equiv. Magnesium 55.48 mg)</td>
</tr>
<tr>
<td>Potassium sulfate</td>
<td>8.92 mg (equiv. Potassium 4 mg)</td>
</tr>
<tr>
<td>Ferrous fumarate</td>
<td>9.13 mg (equiv. Iron 3 mg)</td>
</tr>
<tr>
<td>Chromium picolinate</td>
<td>50 mcg (equiv. Chromium 6.20 mcg)</td>
</tr>
<tr>
<td>Manganese amino acid chelate</td>
<td>12 mg (equiv. Manganese 1.2 mg)</td>
</tr>
<tr>
<td>Copper gluconate</td>
<td>200 mcg (equiv. Copper 28 mcg)</td>
</tr>
<tr>
<td>Potassium iodide</td>
<td>66 mcg (equiv. Iodine 50 mcg)</td>
</tr>
<tr>
<td>Zinc amino acid chelate</td>
<td>30 mcg (equiv. Zinc 6 mcg)</td>
</tr>
<tr>
<td>Selenomethionine</td>
<td>65 mcg (equiv. Selenium 26 mcg)</td>
</tr>
<tr>
<td>Ubidecarenon</td>
<td>1 mg (Co-enzyme Q10)</td>
</tr>
</tbody>
</table>

RDI, recommended daily intake.
the past week.” The DASS is considered suitable for normal populations as some experience of such symptoms is normal in day-to-day life.

**Perceived Stress Scale (Cohen et al. 1983)**

This questionnaire has 14 items designed to measure a respondent’s perception of stress. The participants are asked to score on a scale of 0–4 how often they have felt a particular way over the past month. Total scores range from 0–56 with higher scores indicating a greater degree of perceived stress and lower scores indicating effective coping.

**Profile of Mood States (McNair et al. 1971)**

The participants indicated on a 5-point scale from 0 (not at all) to 4 (extremely) the degree to which they have identified with each of 65 mood-related adjectives within the past week. Items are summed into six factors; Tension–Anxiety, Confusion–Bewilderment, Vigor–Activity, Anger–Hostility, Depression–Dejection, and Fatigue–Inertia. A total mood disturbance score is computed as the sum of the first five factors minus Vigor–Activity. High scores indicate greater mood disturbance on all scales except Vigor–Activity.

**Visual Analog Mood Scales**

This questionnaire, based on the original scale by Bond and Lader (1974), is a measure of subjective mood experience at the present moment. It required participants to mark the appropriate position on a 100 mm horizontal line separating two adjective pairs, such as Happy–Sad or Sociable–Withdrawn. Positive adjectives were aligned to the left. Stroke distance from the left (mm) is manually calculated for the 16 items, and total score was the mean distance from the left. Lower scores indicate more desirable mood states. There are three subscales to the questionnaire, representing the factors “Alert”, “Content”, and “Calm”.

**Procedure**

Testing took place at a dedicated research laboratory. The participants were assessed individually. During the baseline assessment, all participants gave written informed consent and were administered the Mini-Mental State Examination (MMSE; Folstein et al. 1975) to screen for cognitive impairment. Height and weight were also measured and Body Mass Index was calculated (kg/m²). The participants then completed the suite of questionnaires described earlier in the text, followed by a computerized cognitive test battery (results of which will be presented elsewhere). They were randomized to either the active (n = 25) or placebo (n = 25) arm. They were instructed to take “one tablet daily, during or immediately after a meal” for the 8 weeks of the trial. They then returned to the laboratory and completed the same set of questionnaires. The participants were asked to return any unused tablets at their post-treatment testing session, and remaining tablets were counted to determine compliance. Following assessment, the participants were thanked and debriefed. On completion of the trial, they were compensated $40 for their participation.

**Statistical analysis**

Data were analyzed using Statistical Package for the Social Sciences for Windows statistical software package v17.0 (IBM Corporation, New York, NY, USA). For the GHQ, PSS, POMS, and VAMS, group scores at baseline were compared using independent samples t-tests to ensure there were no pre-existing group differences. Change from baseline scores were then computed for each outcome, and these change scores were compared between treatment groups using independent samples t-tests. For the DASS scores, the data were significantly positively skewed; therefore, the non-parametric equivalent (Mann–Whitney U-test) was used to compare both baseline and change from baseline scores. The significance level was set at p < 0.05.

**RESULTS**

**Demographic and morphometric data**

The two groups were well matched for age [Multivitamin Group: M = 62.1, SD = 3.8; Placebo Group: M = 62.9, SD = 7.0], MMSE score [Multivitamin Group: M = 29.3, SD = 0.7; Placebo Group: M = 28.7, SD = 1.5], and years of education [Multivitamin Group: M = 14.3, SD = 2.8; Placebo Group: M = 14.7, SD = 2.8]. Independent sample t-tests indicated that there were no significant differences between the groups on these variables (p-values > 0.05).

**Health and mood assessments**

Means and standard deviations for each of the mood measures are presented in Table 2. Independent sample t-tests of the GHQ, PSS, POMS, VAMS, and Mann–Whitney U analysis of the DASS scores, indicated that there were no significant group differences at baseline for any of these measures or their subscales.

**General Health Questionnaire**

There was a significant group difference for GHQ scores [t(47) = 2.508, p = 0.016]. The change from baseline in
the multivitamin group was significantly higher than that in the placebo group.

**Depression, Anxiety, and Stress Scale**

There was a significant treatment effect for the total DASS score ($z = 2.131, p = .033$), but not for any of the subscales on this measure.

**Perceived Stress Scale and Profile of Mood States**

There were no significant Treatment effects for scores on the PSS or on the POMS for the total score or for the subscales after either treatment.

**Visual analog mood scales**

There were significant group differences in the change from baseline Alert scores, with the multivitamin group having significantly more positive change scores ($t(47) = 2.210, p = .032$). There were no other significant group differences except for a trend for better performance in the multivitamin group on the overall VAMS scores ($t(47) = 1.805, p = .078$).

DISCUSSION

In the present study, an 8-week course of a multivitamin supplement containing vitamins, minerals, antioxidants, and herbal extracts resulted in a number of significant changes in a group of older men, when compared with placebo. Specifically, multivitamin supplementation improved negative mood symptoms and subjective mood. Analysis of the DASS data revealed significant reductions in overall score, but not in subscales measuring symptoms of depression, anxiety, or stress. The GHQ substantiated these findings, with an overall reduction in scores in the multivitamin group compared with placebo, indicating that the participants who supplemented with the multivitamin reported fewer symptoms of mood disorder and/or fewer problems with their day-to-day functioning. In addition, results from the VAMS revealed that the participants in the multivitamin group felt a more positive mood experience after supplementing.

Our results are broadly consistent with the findings of Gariballa and Forster (2007a, 2007b), who found a
reduction in depressive symptoms with multivitamin supplementation in hospitalized elderly. The present study suggests that this type of supplementation may be appropriate for a wider population, as our findings were observed in non-institutionalized, healthy older men. In another study, America and Milling (2008) attributed reductions in depressive symptoms in healthy young adults to a placebo effect, as similar reductions were demonstrated across treatment groups. In the present study, there were no changes in the placebo group, signifying a real effect of multivitamin supplementation. Taken together, these studies may argue for a benefit of supplementation for older adults rather than younger adults, however, differences in composition among multivitamin preparations may also give rise to inconsistent results. The present findings are, particularly, relevant for older people who may be at risk of experiencing subclinical depressive symptoms (Chachamovich et al. 2008).

The findings also share some similarities with the Kennedy et al. (2010) 33-day study in healthy young adults, where improved GHQ scores were associated with the active treatment. On the other hand, they also found improvements on the PSS and the Vigor scale of the POMS (and marginally significant improvements to the confusion subscales and total POMS score). Unlike the present study, Kennedy et al. reported no effects of supplementation on the Bond–Lader VAMS. It may be that these differences reflect real differential effects on younger and older men. On the other hand, we cannot rule out the possibility of methodological differences (for example the duration of treatment was approximately twice as long in the current study), or that differences in the levels of vitamins in the treatments may have contributed to the effects.

In the present study, there were no significant changes in the POMS, although there was a reduction in scores in the multivitamin group after supplementation. The variation between subjects was large on this scale, which may have made it difficult to gain significance with small observed changes. The POMS questionnaire deals with fewer clinical issues than the DASS. The POMS deals with participants identifying with adjectives that include negative feelings and moods; the DASS relates more specifically to clinical symptoms: depression, anxiety, and stress. Therefore, it is interesting to note that the DASS instrument shows a statistically robust effect, whereas the POMS, no effect. These findings suggest that multivitamin supplementation may specifically improve clinical mood disorder symptoms as the DASS was designed to screen for these, but not more general disturbed mood as measured by the POMS.

No changes were observed on the PSS, which is consistent with the DASS Stress subscale, and indicates that the supplement did not affect the participants’ experiences of stress.

There are a number of ingredients in the multivitamin supplement that have the potential to elicit the improvements observed in this study. For example, there is a well-documented association between folate and clinical mood disorders (Bottiglieri 2005), which may also be relevant in non-clinical populations (Malouf et al. 2003). Improved mood has been observed in older people after supplementation with vitamin C (Smith 1999) and vitamin D (Dumville et al. 2006). The herbal ingredients in the supplement may also have played a role. Ginseng and Ginkgo biloba are reportedly used for stress reduction and mood enhancement (Skidmore-Roth 2010), whereas gotu kola has been observed to improve alertness and calmness in healthy elderly participants (Wattanathorn et al. 2008).

Other constituents in the multivitamin supplement that are known to have bearing on brain mechanisms in general may have contributed to the current findings. For example, antioxidants such as vitamin C, E, and flavonoids maintain a redox balance and can reduce oxidative stress (Glade 2010), zinc has both antioxidant and anti-inflammatory properties (Bao et al. 2010), α-tocopherol and vitamin D are involved with regulation of cellular proliferation, differentiation, and apoptosis (Singh and Jialal 2004; Holick 2007) and the antioxidant and anti-inflammatory properties of multivitamins have been linked to increased telomere length of leukocyte DNA (Xu et al. 2009).

The present study investigated the effects of a multivitamin formulation on mood and stress in older men, thus the findings cannot be extended to women. Furthermore, the study observed chronic effects after several weeks of supplementation and did not consider possible additional acute effects. For example, acute mood improvements have been observed after ingestion of a multivitamin, mineral, and guarana supplement (Kennedy et al. 2008), and after consumption of a cocoa drink containing antioxidant flavanols (Scholey et al. 2010). One further issue is the extent to which background diet may modulate the effects seen here. Kennedy et al. found that when habitual fruit and vegetable intake were incorporated into their analysis, one further measure was significantly improved by multivitamin supplementation (Kennedy et al. 2010). In the present study, the participants were instructed to maintain their usual diet but no record of habitual intake was taken. We cannot rule out the possibility that these effects may have been more pronounced in individuals who routinely consume a diet low in...
vitamins and minerals (or indeed less evident in those with higher intakes). Furthermore, the sample was relatively small; a larger study is required to confirm and possibly strengthen the present findings.

Overall, the current study investigated the effects of a multivitamin supplement containing minerals, antioxidants and herbal extracts on mood in older men. The results suggest that multivitamin supplementation may be useful in improving alertness and reducing negative mood symptoms and improving day-to-day functioning.

DECLARATION

The research presented in this report was conducted in accordance with the Declaration of Helsinki, 1975 as revised in 1983. It was approved by the Swinburne University Human Research Ethics Committee.

FUNDING ACKNOWLEDGEMENTS

Swisse Vitamins Pty Ltd provided the multivitamin and placebo tablets as well as partial funding for this project, but played no role in the study design, conduct of trial, analysis and interpretation of data, or writing of this report.

CONFLICT OF INTEREST

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REFERENCES


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