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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.

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; Baldewicz *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

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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 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 Swisse 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,

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

	Supplement	RDI
Vitamin E (d-alpha-tocopheryl acid succinate)	41.33 mg	10 mg
Vitamin B1 (thiamine hydrochloride)	30 mg	1.2 mg
Vitamin B2 (riboflavin)	30 mg	1.3 mg
Vitamin B3 (nicotinamide)	30 mg	16 mg
Vitamin B5 (calcium pantothenate)	70 mg (equiv. Pantothenic Acid 64.13 mg)	6 mg
Vitamin B6 (pyrodoxine hydrochloride	30 mg	1.7 mg
Vitamin B12 (cyanocobalamin)	30 mcg	2.4 mcg
Biotin	50 mcg	30 mcg
Folic acid	500 mcg	400 mcg
Calcium ascorbate dihydrate	200 mg (equiv. Ascorbic acid (Vitamin C) 165.2 mg)	45 mcg
Choline bitartrate	25 mg	
Inositol	25 mg	
Bioflavonoids	40 mg	
Lysine hydrochloride	50 mg	
Tyrosine	1 mg	
Calcium citrate	100 mg (equiv. Calcium 21 mg)	1300 mg
Magnesium oxide – heavy	100 mg (equiv. Magnesium 55.48 mg)	420 mg
Potassium sulfate	8.92 mg (equiv. Potassium 4 mg)	3800 mg
Ferrous fumarate	9.13 mg (equiv. Iron 3 mg)	8 mg
Chromium picolinate	50 mcg (equiv. Chromium 6.20 mcg)	35 mcg
Manganese amino acid chelate	12 mg (equiv. Manganese 1.2 mg)	5.5 mg
Copper gluconate	200 mcg (equiv. Copper 28 mcg)	1.7 mg
Potassium iodide	66 mcg (equiv. Iodine 50 mcg)	150 mcg
Zinc amino acid chelate	30 mg (equiv. Zinc 6 mg)	14 mg
Selenomethionine	65 mcg (equiv. Selenium 26 mcg)	70 mcg
Ubidecarenon	1 mg (Co-enzyme Q10)	

RDI, recommended daily intake.

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

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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/m^2). 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

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Table 2. Results of questionnaire scores for multivitamin and placebo groups at baseline and after 8 weeks of supplementation

	Multivitamin			Placebo			Test statistic	*p*	Cohen's d
	Baseline	Post-treatment	Change score	Baseline	Post-treatment	Change score	*T*		
GHQ	36 ± 12	31 ± 13	−4.7 ± 10.9	34 ± 11	36 ± 16	2.8 ± 8.1	2.508	**0.016**	0.463
PSS	18.000 ± 8.000	17.400 ± 7.000	−0.800 ± 4.900	17.000 ± 9.000	17.500 ± 9.200	0.600 ± 6.700	0.786	0.436	0.239
POMS									
Total	14.800 ± 35.600	8.600 ± 24.700	−7.300 ± 19.100	10.700 ± 29.500	15.700 ± 34.200	2.900 ± 25.600	1.594	0.118	0.465
Tension–Anxiety	6.800 ± 6.000	6.100 ± 5.000	−1.000 ± 3.700	5.200 ± 4.800	6.200 ± 5.000	0.500 ± 4.200	1.315	0.195	0.384
Depression–Dejection.	5.400 ± 7.100	4.400 ± 5.400	−1.200 ± 4.800	6.000 ± 8.700	6.000 ± 7.400	−0.900 ± 4.800	0.345	0.732	0.101
Anger–Hostility	7.200 ± 8.200	5.200 ± 5.600	−2.300 ± 5.300	6.300 ± 8.100	7.200 ± 8.800	0.200 ± 4.400	1.838	0.072	0.536
Vigor–Activity	18.400 ± 7.000	18.500 ± 5.600	0.000 ± 5.100	18.200 ± 6.100	17.600 ± 6.900	−0.500 ± 4.900	0.317	0.753	0.090
Fatigue–Inertia	6.800 ± 6.100	6.000 ± 4.100	−1.100 ± 5.900	5.500 ± 4.200	6.000 ± 4.800	0.600 ± 4.000	1.147	0.257	0.335
Confusion–Bewilderment	5.600 ± 4.900	4.500 ± 2.900	−1.300 ± 3.400	5.700 ± 4.200	5.500 ± 4.200	−0.400 ± 3.100	1.040	0.304	0.304
VAMS									
Total	26.700 ± 12.900	22.700 ± 11.600	−3.900 ± 8.700	24.900 ± 11.000	26.400 ± 14.500	1.600 ± 11.400	1.805	0.078	0.527
VAMS Alert	29.400 ± 16.300	24.200 ± 13.900	−5.200 ± 9.600	25.600 ± 11.900	27.600 ± 15.800	2.000 ± 12.600	2.210	**0.032**	0.477
VAMS Content	26.800 ± 14.900	23.700 ± 13.300	−3.200 ± 12.000	24.700 ± 14.100	25.500 ± 17.800	0.900 ± 13.400	1.135	0.262	0.331
VAMS Calm	28.800 ± 14.100	26.500 ± 14.600	−2.300 ± 12.100	22.200 ± 13.100	23.500 ± 14.200	1.400 ± 15.000	1.009	0.318	0.294
DASS							*Z*		
Total	8.500 ± 6.300 (7)	5.700 ± 5.000 (5)	−2.800 ± 3.600	7.300 ± 8.000 (4)	5.600 ± 4.800 (5)	−1.300 ± 6.100	2.131	**0.033**	0.301
Depression	2.800 ± 3.400 (2)	1.400 ± 2.000 (1)	−1.400 ± 2.400	2.700 ± 3.800 (1)	2.200 ± 2.700 (1.500)	−0.500 ± 2.300	1.172	0.241	0.393
Anxiety	1.500 ± 1.400 (1)	0.600 ± 0.700 (0)	−0.600 ± 1.100	1.200 ± 1.800 (1)	0.700 ± 1.000 (0.500)	−0.500 ± 2.100	1.317	0.188	0.064
Stress	4.200 ± 3.200 (4)	3.100 ± 2.700 (3)	−1.100 ± 2.400	3.000 ± 2.700 (2)	2.600 ± 2.200 (2)	−0.400 ± 2.400	0.870	0.384	0.299

Means (± SD) are shown along with summary statistics from *t*-tests of change-from-baseline data for GHQ, PSS, POMS, and VAMS.
For the DASS non-parametric Mann–Whitney *U*-tests were used, median values are shown in parentheses and *p*-values reflect comparisons of change-from-baseline scores between multivitamin and placebo arms (see text).
Effects sizes (Cohen's d) for treatment differences in change-from-baseline scores are also presented.
All significant differences are shown in bold, *, $p < 0.05$.
GHQ, General Health Questionnaire; PSS, Perceived Stress Scale; POMS, Profile of Mood States; VAMS, Visual Analog Mood Scales; DASS, Depression, Anxiety and Stress Scale.

the multivitamin group was significantly higher than that in the placebo group.

Depression, Anxiety, and Stress Scale

There was a significant treatment effect *x* time 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

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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

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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.

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CONFLICT OF INTEREST

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REFERENCES

Alpert JE, Mischoulon D, *et al*. 2000. Nutrition and depression: focus on folate. *Nutrition* **16**(7–8): 544–546.

America A, Milling LS. 2008. The efficacy of vitamins for reducing or preventing depression symptoms in healthy individuals: natural remedy or placebo? *J Behav Med* **31**: 157–167.

Baldewicz TT, Goodkin K, *et al*. 2000. Cobalamin level is related to self-reported and clinically rated mood and to syndromal depression in bereaved HIV-1+ and HIV-1- homosexual men. *J Psychosom Res* **48**(2): 177–185.

Bao B, Prasad AS, *et al*. 2010. Zinc decreases C-reactive protein, lipid peroxidation, and inflammatory cytokines in elderly subjects: a potential implication of zinc as an atheroprotective agent. *Am J Clin Nutr* **91**(6): 1634–1641.

Benton D. 2002. Selenium intake, mood and other aspects of psychological functioning. *Nutr Neurosci* **5**(6): 363–374.

Bond A, Lader M. 1974. The use of analogue scales in rating subjective feelings. *Br J Psychol* **47**: 211–218.

Bottiglieri T. 2005. Homocysteine and folate metabolism in depression. *Prog Neuro-Psychoph* **29**(7): 1103–1112.

Carroll D, Ring C, *et al*. 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* **150**(2): 220.

Chachamovich E, Fleck M, *et al*. 2008. Impact of major depression and subsyndromal symptoms on quality of life and attitudes toward aging in an international sample of older adults. *Gerontologist* **48**(5): 593–602.

Cockle SM, Haller J, *et al*. 2000. The influence of multivitamins on cognitive function and mood in the elderly. *Aging Ment Health* **4**: 339–353.

Cohen S, Kamarck T, *et al*. 1983. A global measure of perceived stress. *J Heal Soc Behav* **24**(4): 385–396.

Dumville JC, Miles JN, *et al*. 2006. Can vitamin D supplementation prevent winter-time blues? A randomised trial among older women. *J Nutr Health Aging* **10**(2): 151–153.

Eisenberg DM, Davis RB, *et al*. 1998. Trends in alternative medicine use in the United States, 1990–1997: results of a follow-up national survey. *JAMA* **280**(18): 1569–1575.

Eisenberg DM, Kessler RC, *et al*. 1993. Unconventional medicine in the United States --prevalence, costs, and patterns of use. *N Engl J Med* **328**(4): 246–252.

Folstein MF, Folstein SE, *et al*. 1975. "Mini-mental state" : a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* **12**(3): 189–198.

Gariballa S, Forster S. 2007a. Dietary supplementation and quality of life of older patients: a randomized, double-blind, placebo-controlled trial. *J Am Geriatr Soc* **55**(12): 2030–2034.

Gariballa S, Forster S. 2007b. Effects of dietary supplements on depressive symptoms in older patients: a randomised double-blind placebo-controlled trial. *Clin Nutr* **26**: 545–551.

Glade MJ. 2010. Oxidative stress and cognitive longevity. *Nutrition* **26**(6): 595–603.

Goldberg DP. 1978. Manual of the General Health Questionnaire. NFER Publishing Company: Windsor, UK.

Holick MF. 2007. Vitamin D deficiency. *N Engl J Med* **357**(3): 266–281.

Hvas A-M, Juul S, et a. 2004. No effect of vitamin B-12 treatment on cognitive function and depression: a randomized placebo controlled study. *J Affect Disord* **81**: 269–273.

Kelly JP, Kaufman DW, *et al*. 2005. Recent trends in use of herbal and other natural products. *Arch Intern Med* **165**(3): 281–286.

Kennedy D, Veasey R, *et al*. 2010. Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males. *Psychopharmacology* **211**: 55–68.

Kennedy DO, Haskell CF, *et al*. 2008. Improved cognitive performance and mental fatigue following a multi-vitamin and mineral supplement with added guarana (Paullinia cupana). *Appetite* **50**(2–3): 506–513.

Kessler RC, Soukup J, *et al*. 2001. The use of complementary and alternative therapies to treat anxiety and depression in the United States. *Am J Psychiatry* **158**(2): 289–294.

Kessler RC, Zhao S, *et al*. 1997. Prevalence, correlates, and course of minor depression and major depression in the national comorbidity survey. *J Affect Disord* **45**(1–2): 19–30.

Levenson CW. 2006. Zinc: the new antidepressant? *Nutr Rev* **64**(1): 39–42.

Lovibond SH, Lovibond PF 1995. Manual for the Depression Anxiety Stress Scales. Psychology Foundation: Sydney, Australia.

MacLennan AH, Wilson DH. 1996. Prevalence and cost of alternative medicine in Australia. *Lancet* **347**(9001): 569.

MacLennan AH, Wilson DH, et a. 2002. The escalating cost and prevalence of alternative medicine. *Prev Med* **35**(2): 166–173.

Malouf R, Grimley Evans J, Areosa Sastre A. 2003. Folic acid with or without vitamin B12 for cognition and dementia. *Cochrane Database of Systematic Reviews* **4**(CD004514): 1–29.

McDowell I. 2006. Measuring Health A Guide to Rating Scales and Questionnaires. Oxford University Press: Oxford.

McNair DM, Lorr M, *et al*. 1971. Manual for the Profile of Mood States (POMS). Educational and Industrial Testing Service: San Diego, CA.

NHMRC. 2005. Nutrient Reference Values for Australia and New Zealand. Commonwealth of Australia: A. G. D. o. H. a. Ageing. Canberra.

Scholey AB, French SJ, *et al*. 2010. Consumption of cocoa flavanols results in acute improvements in mood and cognitive performance during sustained mental effort. *J Psychopharmacol* **24**(10): 1505–1514.

Singh U, Jialal I. 2004. Anti-inflammatory effects of alpha-tocopherol. *Ann N Y Acad Sci* **1031**: 195–203.

Skidmore-Roth L. 2010. Mosby's Handbook of Herbs and Natural Supplements. Elsevier Health Sciences: St. Louis, Mo.: Mosby/Elsevier.

Smith AP. 1999. Vitamin C, mood and cognitive functioning in the elderly. *Nutr Neurosci* **2**(4): 249–256.

Stanger O, Fowler B, *et al*. 2009. Homocysteine, folate and vitamin B12 in neuropsychiatric diseases: review and treatment recommendations. *Expert Rev Neurother* **9**(9): 1393–1412.

Tolmunen T, Voutilainen S, *et al*. 2003. Dietary folate and depressive symptoms are associated in middle-aged Finnish men. *J Nutr* **133**(10): 3233–3236.

Wattanathorn J, Mator L, *et al*. 2008. Positive modulation of cognition and mood in the healthy elderly volunteer following the administration of *Centella asiatica*. *J Ethnopharmacol* **116**(2): 325–332.

Wilkins CH, Sheline YI, *et al*. 2006. Vitamin D deficiency is associated with low mood and worse cognitive performance in older adults. *Am J Geriatr Psychiatry* **14**(12): 1032–1040.

Williams A-l, Cotter A, *et al*. 2005. The role for vitamin B-6 as treatment for depression: a systematic review. *Fam Pract* **22**(5): 532–537.

Xu Q, Parks CG, *et al*. 2009. Multivitamin use and telomere length in women. *Am J Clin Nutr* **89**(6): 1857–1863.

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