A Beneficial Effect of Calcium Intake on Mood

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Abstract

Two experiments were conducted to test the hypothesis that the intake of supplementary calcium elevates mood. A total of 123 student volunteers without a previous diagnosis of depressive disorders received either placebo or calcium (1000 mg) tablets. The tablets were taken for a period of four weeks, one tablet, twice per day. In Experiment 1, mood was assessed at two times: Once before the start of calcium intake and another time after four weeks of calcium intake. The supplementary intake of calcium, compared to placebo, was associated with significantly greater elevation in mood as measured by the Beck Depression Inventory. In Experiment 2, mood was assessed before, two weeks after, and four weeks after calcium intake, as well as a fifth time, one week after the discontinuation of calcium intake. As in the first experiment, calcium, in contrast to placebo, produced a significantly greater elevation in mood. The results of these experiments show a beneficial effect of calcium on mood and suggest a possible use for the treatment of depressive disorders.

It has been known for many decades that calcium plays an important role in neuronal activity, and the list of neuronal processes found to be mediated by calcium continues to grow. Because neuronal activity influences cognitive and behavioral variables, the discoveries of the different neuronal effects of calcium are of great significance to the sciences of mind and behavior. This is especially evident in the instances that calcium affects neuronal processes specifically associated with particular mental or behavioral phenomena. One such instance is represented by the finding that calcium influences the activity of the neurons that are theorized to mediate mood.

Monoaminergic neurons have been theorized to mediate mood and emotions. There is a variety of evidence that suggest the involvement of these neurons in mood and emotions. Electrical stimulation of these pathways, for example, are associated with the production of reward (Crow, Spear, & Arbuthnott, 1972; Gallistel, Shizgal, & Yeomans, 1981; Stein, 1968). Pharmacological treatments that increase monoaminergic activity produce an antidepressant effect (Goodwin, Murphy, Brodie, & Bunney, 1970; Jouvent et al., 1977; van Praag, 1979; Willner, 1983). Pharmacological treatments that decrease the activity of these neurons produce a depressant effect (Fries, 1954; Randrup et al., 1975; Raskin, Schulterbrandt, Reatig, & McKeon, 1970). Additionally, many antidepressants have been shown to increase monoaminergic activity (e.g., See Carlsson, 1961; McNeal & Cimbolic, 1986; Murphy et al., 1981; Potter, Rudorfer, & Manji, 1991). Finally, in some subtypes of depressive illness monoaminergic activity is reduced (Mass, Fawcett, & Dekirmenjian, 1972; van Praag, Korf, & Schut, 1973; Schildkraut, 1965; Sjostrom, 1973).

On the other hand, calcium has been found to affect the activity of these neurons. Calcium-dependent calmodulin, for example, increases the synthesis of monoamines (Kuhn & Lovenberg, 1982). Large increases in the extracellular calcium have been reported to dramatically decrease the activity of monoaminergic neurons (Trulson & Crisp, 1985). Also, the release of the neurotransmitters depends on the entry of calcium into the nerve terminal (Katz & Miledi, 1970). Moreover, it is hypothesized that the postsynaptic effect of the monoamines is mediated by a calcium-dependent mechanism (Phillis, 1974).

More direct evidence of a role for calcium in mood is also available. For instance, in animal models of depression, large increases of calcium levels have been associated with decreases in escape response (Trulson, Arasteh, & Ray, 1986), and the administration of a calcium agonist has decreased mobility (Mogilnicka, Czyrak, & Maj, 1988). Furthermore, Mogilnicka et al. (1988) were

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able to block the effect by the administration of a calcium-channel blocker. In humans, some conditions that are associated with changes in calcium metabolism (e.g., hypercalcemia and hyperparathyroidism) are also accompanied by changes in mood (Cogan et al., 1978; Mandel, 1960; Rein-frank, 1961) and mood disorders are associated with altered levels of intracellular calcium (Dubovsky, Murphy, Thomas, & Rademacher, 1992). Finally, some studies have reported successful treatment of patients with bipolar depressive illness by using organic calcium-channel blockers (e.g., Dubovsky, Franks, Lifschitz, & Coen, 1982; Caillard et al., 1982; Garza-Trevifio, Overall, & Hollister, 1992).

These findings suggest that changes in calcium levels are closely related to alterations in mood. Moreover, there appears to be a biphasic effect such that slight increases in calcium levels seem to be associated with improvement in mood, whereas very large increases are associated with the opposite effect.

The two studies presented here were conducted to provide an experimental investigation of the effect of relatively small increases in calcium levels over a period of four weeks. It was hypothesized that the intake of dietary calcium supplement would result in an improvement in mood.

Experiment 1

Method

Participants. Forty seven male and female university students enrolled in the introductory psychology course were recruited for the study in exchange for receiving credit towards the fulfillment of their course requirements. Subjects did not have a history of calcium-related disorders and were not taking calcium supplements prior to the study. They were informed about the experimental procedures and their consent was obtained.

Calcium Tablets. Calcium tablets were composed of 1000 mg of calcium and 600 IU of vitamin D. This amount of supplement has been shown to be effective in producing cardiovascular change, perhaps due to the ability to block calcium channels (McCarron, 1985; McCarron, Morris, & Cole, 1982). The addition of vitamin D is necessary for the absorption of calcium from the intestinal tract. Placebo tablets were similar to calcium tablets in appearance, but were composed of gelatin and filler.

Measures. Two measures were used in the assessment of mood: The BDI (Beck, 1978), and the Zung Self-Rating Depression Scale (SDS;Zung, 1965). The **BDI** consists of 21 items derived from clinical observation. The possible scores on this measure range from 0 to 63. Scores of 9 or below are considered to be asymptomatic and scores of 10 to 18 are considered to be associated with mild/ moderate depression (Beck and Steer, 1987). Scores higher than 18 indicate severe depression. The SDS consists of 20 items. The possible raw scores range from 20 to 80, and scores of 40 or above are considered to be indicative of clinical depression.

Design. A double-blind, factorial design with random assignment of treatment levels was used. Subjects were divided into two mood groups, "non-depressed," and "depressed" according to their initial BDI scores. Subjects in each group were then randomly assigned to one of the two treatment levels (i.e., placebo or calcium). Each subject was tested at two times.

Procedure. The experiment was conducted in two sessions. At the start of the first session, the participants received information about the protocol and their consent was obtained. Subsequently, the BDI and SDS were administered. The BDI scores of the participants were then used to divide them into the two mood groups of "non-depressed" (BDI 9) and "depressed" (BDI 10). These cut-off scores were used following the guidelines suggested by Beck and Steer (1987). Using a random number table, the participants within each mood group were then assigned to either the calcium or placebo groups (in keeping with the double-blind nature of the experiment, scales, questionnaires, and tablet vial of each individual were identified by ID numbers only). One day after the first session, the participants were given a four-week supply of the appropriate tablets in an unlabeled vial and were told to take one tablet, twice per day over the following four weeks. After four weeks the BDI and the SDS were administered again and the subjects were debriefed about the

nature of the experiment.

Results

Two dependent measures, BDI and SDS, were calculated for each subject by subtracting their BDI and SDS scores of the first session from those of the second session. Factors were calcium (i.e., whether the subject had received calcium or placebo tablets) and mood (i.e., "non-depressed" when the subject had an initial BDI score of 9 or less, and "depressed" when the subject had an initial BDI score of 10 or greater). Data were analyzed by the SPSS procedure for ANOVA. There was a significant effect of calcium on BDI ($F(1, 33) = 4.58$, $p < .05$). The mean decrease in the BDI score of the calcium group was 3.05 (SD=2.39) in comparison to 1.33 (SD=3.12) of the placebo group. These changes meant that the mean BDI score of the calcium group had changed from 5.47 (SD=3.27) to 2.42 (SD=2.59), while the mean BDI score of the placebo group had changed from 6.06 (SD=4.21) to 4.72 (SD=3.88). Also, there was a significant effect of mood ($F(l, 33) = 9.07$, $p < .01$) on BDI. The mean decrease in the BDI score of the "depressed" group was 4.29 (SD=4.07) in contrast to 1.73 (SD=2.35) of the "non-depressed"group. However, there was no interaction effect on BDI. Calcium did not have any significant effect on SDS. However, the mean decrease in the SDS scores was greater for the calcium group (X=2.73, SD=3.0) than for the placebo group (X=l .0, SD=6.45). Also, the effect of mood on SDS approached significance ($F(1, 33) = 3.07$, $p < .1$). The mean decreases in the SDS scores were 1.07 (SD=4.83) for the "non-depressed" group and 4.43 (SD=4.93) for the placebo group.

Experiment 2

Method

Participants. Seventy six male and female university students enrolled in the introductory psychology course were recruited for the study in exchange for receiving credit towards the fulfillment of their course requirements. Subjects did not have a history of calcium-related disorders and were not taking calcium supplements prior to the study. They were informed about the experimental procedures and their consent was obtained.

Calcium Tablets. The same tablets as in Experiment 1 were used.

Measures. As in Experiment 1 the BDI was used. However SDS was replaced with the Depression Adjective Check List (DACL), which may be more appropriate for measuring changes in mood in non-clinical populations. The DACL is a list of 32 adjectives, 10 of which are associated with the absence of depression and 22 of which are associated with depression. The possible scores on this scale range from 0 to 34. Higher scores are associated with greater severity of mood.

Design. Same design as in Experiment 1 was implemented, with the exception that each subject was tested at four times.

Procedure. The experiment consisted of four sessions. Session procedures were similar to Experiment 1 and the same methods were used to assign the subjects to groups. One day after the first session, the participants were given a two-week supply of the appropriate tablets in an unlabeled vial and were told to take one tablet, twice per day over the following two weeks.

Two weeks after the start of the experiment the participants were again administered the BDI and DACL . At the end of the session each participant received another vial containing a two-week supply of their tablets, and the appropriate instructions.

Four weeks after the start of the experiment, the scales were administered a third time and the participants discontinued their intake of the tablets.

The scales were administered a final time at five weeks, and at the end of the session the participants were debriefed about the nature of the experiment.

Results

Two dependent measures, BDI and DACL, were calculated for each session of each of the subjects by subtracting the BDI and DACL scores of session 1 from those of session 2, 3, and 4. Data were analyzed using the SPSS univariate procedure for MANOVA with repeated measures. Calcium produced a significant overall difference in the BDI ($F(1, 47) = 4.47$, $p < .05$). Several patterns in the data were observed.

First, during the period of supplement intake, the mean decrease in the BDI scores of the calcium group was 5.35 (SD=5.64) in contrast to 2.92 (SD=3.99) of the placebo group. These changes meant that the mean BDI score of the calcium group had changed from 8.65 (SD=7.07) to 3.31 (SD=3.11), while the mean BDI score of the placebo group had changed from 7.96 (SD=6.55) to 5.04 (SD=6.78). Moreover, during the same time period, the mean BDI score of the "depressed" subjects in the calcium group changed from 17.0 (SD=8.21) to 5.57 (SD=3.41), a change of 11.43 points, while that of the "depressed"subjects in the placebo group changed from 16.33 (SD=8.55) to 12.33 (SD=10.46), a change of 4.0 points. In addition to the effect of calcium, mood produced a significant difference in the BDI ($F(1, 47) = 11.39$, $p < .005$). For the duration of the study, the mean decrease in the BDI score of the "depressed" group was 7.0 (SD=7.87) in contrast to 3.13 (SD=2.88) for the "non-depressed" group. Additionally, the interaction between calcium and mood produced a significant effect in BDI scores ($F(1, 47) = 4.76$, $p < .05$). However, the post-hoc analysis did not show any significant difference between the groups at each session. Calcium did not have any significant effect on the DACL. However, the mean decrease in the DACL scores was greater for the calcium group (X=2.89, SD=6.81) than for the placebo group (X=1.12,SD=6.54). No significant effect of mood was observed for the DACL scores.

General Discussion

The results of the two studies presented here are consistent with the hypothesis that intake of supplemental dietary calcium can improve mood. In both studies calcium significantly decreased the BDI scores, and the effect size was similar in both studies. Moreover, in Experiment 2 the effect of calcium in the "depressed" group was such that the BDI scores decreased from a mean of 17.00, which is associated with moderate depression, to a mean of 5.57, which is well below the cut-off score for mild depression. This is in contrast to the placebo group, in which the BDI scores decreased from a mean of 16.33 to 12.33, a score that is associated with mild depression. In a clinical population, such a difference will be important.

Although the changes in SDS and DACL scores were in the direction predicted by the experimental hypothesis, calcium did not significantly affect either SDS or DACL scores. It is possible that these scales are less sensitive than the BDI to changes in mood, or at least to a subset of changes in mood that may be induced by calcium, and therefore failed to register these mood alterations. This possibility seems more plausible, because the BDI is considered to be more sensitive to changes across time and drug treatment trials (Mayer, 1977). However, the SDS items are very similar to the BDI items. In both scales there are face-valid items that are designed to assess 1) depressed feeling, 2) hopelessness, 3) indecisiveness 4) dissatisfaction, 5) suicidal ideation, 6) irritability, 7) weight loss, 8) loss of libido, 9) loss of appetite, 10) sleep disturbance, 11) somatic preoccupation, 12) crying, and 13) fatigability. The BDI items also include those that measure social withdrawal, and body image changes, symptoms that are not directly assessed by the SDS. The latter, on the other hand, includes items that measure confusion and agitation, which are not directly measured by the BDI. Also, the proportion of variance in one scale that is accounted for by the other is generally low (Kerner & Jacobs, 1983). The correlations reported for DACL and BDI are generally of lower magnitude (Lubin, 1981) than those for SDS and BDI (Beck and Steer, 1987). Although it is difficult to judge the apparent overlap of the DACL and BDI, because of the superficial dissimilarity of the scales.

In addition to answering the general question of whether calcium can improve mood, the time course of the calcium effect was investigated in Experiment 2. However, because at each specific session the differences between the calcium and placebo groups did not reach significance, no conclusions could be drawn in this regard. Therefore, the time course of the effect remains to be examined.

One improvement can be made in future studies by monitoring the blood-level for ionic calcium to provide both a measure of subject compliance for the intake of the supplements, and a covariate for the outcome measure. Also, the inclusion of a

waiting control group will be useful as an index for comparing the extent of the effect of placebo with that of calcium.

In conclusion, it is clear that if the results of this study are supported by others, there will be significant implications regarding mood and possibly the treatment of mood disorders. The latter possibility is strengthened by the isolated reports of successful treatment of depressive illness by calcium-channel blockers (Dubovsky et al., 1982; Caillard et al., 1982) and the recent finding of the effectiveness of supplemental dietary calcium in treatment of the affective symptoms of the menstrual cycle (Alvir & Thys-Jacobs, 1991; Penland & Johnson, in press).

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