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Drinking Spring Water and Lithium Absorption: A Preliminary Study

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Abstract

Background: In Japan, there are several resorts with cold springs that have mineral water containing relatively high levels of lithium compared to tap water. Visitors to such cold-spring resorts traditionally drink 2 to 4 L of mineral water for several hours in the early morning in the belief that the water has properties which maintain physical health. The present study aimed to investigate whether drinking the water increase serum lithium levels despite frequent urination, and to examine the mental effects of drinking mineral water containing lithium and related factors.
Methods: Forty three subjects who were not psychiatrically ill gave informed consent to this study. Before and just after drinking the water, serum lithium levels, the State-Trait of Anxiety Inventory (STAI) scores, Profiles of Mood States Test (POMS) scores and brain-derived neurotrophic factor (BDNF) levels were measured.
Results: The subjects drank 3.64 L of the water in the early morning. Serum lithium levels were significantly increased from 0.026 to 0.073 mEq/L, which were much lower than the ones used in the treatment of psychiatric disorders. After drinking, most ratings of POMS significantly improved. Serum lithium levels were positively and significantly associated with serum BDNF levels, and changes in serum BDNF were negatively and significantly associated with changes in STAI state scores.
Conclusion: The present findings suggest that drinking mineral water containing very low lithium levels may increase serum lithium levels and improve mental state as a likely consequence of changes in BDNF levels, although improvement in subjective well-being may have been due to placebo effect. Taking several methodological limitations into consideration, further studies are required to confirm this suggestion (German J Psychiatry 2008; 11: 103-106).

Keywords: lithium, mineral water, cold spring, STAI, POMS, BDNF

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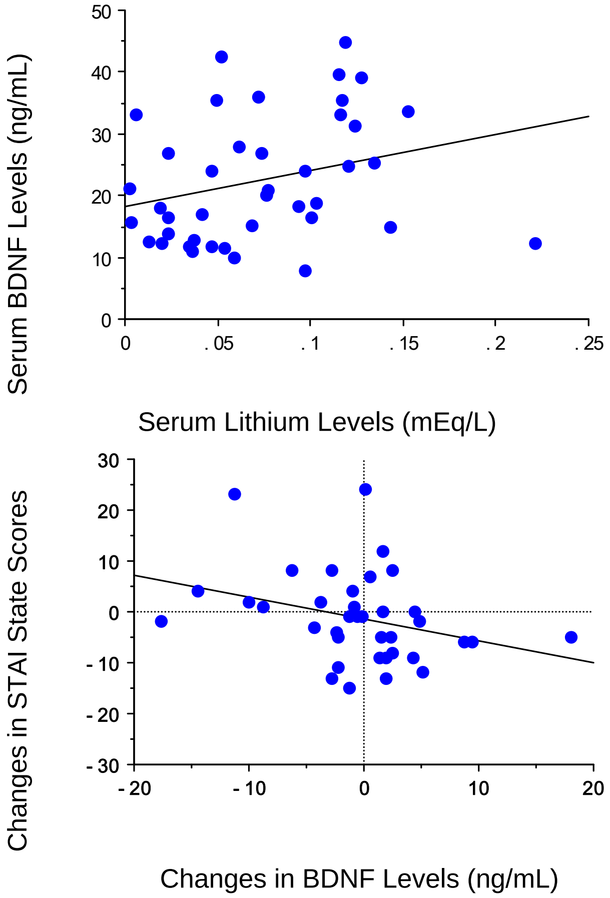
Introduction

Several meta-analyses have confirmed the efficacy of lithium in the treatment of bipolar disorder (Poolsup et al., 2000; Geddes et al., 2004), augmentation of antidepressants (Bauer & Dopfmer, 1999), and suicide (Cipriani et al., 2005). Beyond these established effects, lithium may have prophylactic effects for dementia (Terao et al., 2006) although this is still controversial. These various effects have been investigated within so-called therapeutic ranges, but there is a possibility that even very low levels of lithium may bring about some psychotropic effects because very small amounts of lithium in tap water (0.07-0.16 mg/L) have been associated with less psychiatric hospitalizations (Dawson et al., 1972) and less suicide and crimes (Schrauzer & Shrestha, 1990). Schrauzer et al. (1994) performed a randomized double-blind placebo-controlled lithium supplementation study (400 μg/day) in a total of 24 subjects with a history of substance dependence. As a result, they found that lithium

Figure 1. The Relationship Between Serum Lithium Levels and Serum BDNF Levels After Drinking Lithium Mineral Water, and the Relationship Between Changes in BDNF Levels and Changes in STAI State Scores



group showed rapid and consistent mood improvement in comparison with placebo group although at that time they could not measure very low serum lithium levels and the mechanism was not investigated. Thereafter, to our knowledge, no researcher reconfirmed their findings.

In Japan, there are several resorts with cold springs that have mineral water containing relatively high levels of lithium compared to tap water. Visitors to such cold-spring resorts traditionally drink 2 to 4 L of mineral water for several hours in the early morning in the belief that the water has properties which maintain physical health. Although those who partake in this health regime may not be aware of the possible psychotropic effects of the spring water, we can investigate the effects of drinking mineral water containing very low level lithium. Moreover, recently, very low serum lithium levels can be measured by using mass spectroscopy.

In the present study, we investigated the effects of drinking mineral water containing lithium on serum lithium levels. Moreover, mental state and brain-derived neurotrophic factor (BDNF) were also investigated because lithium has been reported to increase BDNF (Manji et al., 2000). The hypothesis was that drinking mineral water containing lithium may increase serum lithium levels and thereby improve mental state as a likely consequence of changes in BDNF levels.

Method

Two typical resorts with cold springs containing relatively high lithium levels near our university were selected. One was Tsukano cold spring with 6.1 mg/L of lithium mineral water and the other was Rokkasako cold spring with 15.7 mg/L of lithium mineral water. These lithium levels were much lower than those in routine clinical settings (e.g., 400 to 1200 mg/day) but much higher than those in tap water (much less than 1 mg/L). In both springs, visitors stay at an inn near the spring for several days. They wake in the very early morning (around 2-3 AM) and continuously drink from the cold spring until 6-7 AM.

Prior to (i.e. the previous evening) and just after drinking spring mineral water, psychological tests including the State-Trait Anxiety Inventory (STAI) and Profiles of Mood States Test (POMS), blood sampling to measure serum lithium levels and brain-derived neurotrophic factor (BDNF) were performed. In addition, serum creatinine was measured as a parameter of renal function.

Serum lithium levels were measured by using mass spectroscopy at a third party (Oita Yakuzaishi Kensa Center). Serum BDNF levels were measured by one of the authors (R.Y.) using a BDNF Emax Immunoassay Kit (Promega, Madison, WI, USA) according to the sandwich ELISA method. He was blind to the psychological findings of the subjects. Intra- and interassay coefficients of variation were 5% and 7%, respectively. The protocol of this study was approved by the Ethics Committee of Oita University Faculty of Medicine. All subjects gave their consent after having been informed of the study's purpose and methods. The subjects also received advice regarding both possible effects and side effects of drinking the mineral water such as lithium toxicity. As to the statistical analyses, Wilcoxon signed-ranks test and Spearman's correlation coefficient were used.

Results

In total, 43 subjects (26 females and 17 males) entered the study. Their mean age was 65.7±10.8 years. According to our semi-structured interview, none of the participants had psychiatric illnesses. The subjects drank 3.64±1.85 L of spring mineral water from 2-3 AM to 6-7 AM and urinated more frequently than usual. After drinking lithium mineral water, body weight was increased but not significantly (57.6±10.0 to 59.3±9.1 kg, $p<0.08$). Serum lithium levels were significantly increased from 0.026±0.032 to 0.073±0.049 mEq/L ($p<0.0001$). Serum creatinine levels were significantly decreased from 0.69±0.17 to 0.64±0.15 mg/dL ($p<0.0001$) whereas serum BDNF levels were unchanged (22.7±11.8 to 22.5±10.2 ng/mL). After drinking the mineral water, tension and anxiety (47.6±7.2 to 45.3±9.2,

$p<0.01$), depression (51.1 ± 7.4 to 48.8 ± 8.0, $p<0.02$), anger and hostility (50.6 ± 12.3 to 47.1 ± 10.1, $p<0.001$), fatigue (46.8 ± 7.6 to 44.0 ± 7.7, $p<0.03$) and confusion (50.8 ± 8.8 to 48.2 ± 9.2, $p<0.01$) scores of the POMS significantly decreased.

Although there was no association between serum lithium and BDNF levels before drinking lithium mineral water, serum lithium levels became positively and significantly associated with plasma BDNF just after drinking (rho=0.35, $p<0.03$) (Figure 1). Figure 1 also shows that changes in serum BDNF levels were negatively and significantly associated with changes in STAI state scores (rho=-0.36, $p<0.03$).

Discussion

Although the subjects urinated more frequently than usual, the mean serum lithium levels were significantly increased from 0.026 to 0.073 mEq/L by drinking cold spring water containing lithium. Nonetheless, this basal value of 0.026 seems to be high compared to the mean lithium level of people who are not in the habit of drinking lithium mineral water which has been found to be around 0.001 (mEq/L) (unpublished data). It is therefore probable that the basal value was already increased by the sustained drinking of lithium mineral water before the study. Despite the significant increase from 0.026 to 0.073 mEq/L, it should be noted that the value of 0.073 mEq/L is still clearly lower than therapeutic lithium levels (e.g., 0.4-1.0 mEq/L). These findings suggest that serum lithium levels do increase modestly but significantly by drinking cold spring water containing lithium despite frequent urination.

With regard to the effects of such low lithium levels, in the present study, most psychological variables of POMS such as tension and anxiety, depression, anger and hostility, fatigue and confusion were significantly decreased following the increase of lithium levels. Placebo effects and/or trace contained in the spring mineral water other than lithium might have affected their mental state. Nonetheless, it seems likely that lithium, at least partially, affected the results because serum lithium levels were positively and significantly associated with serum BDNF levels (Figure 1), and changes in serum BDNF levels were negatively and significantly associated with STAI state scores (Figure 1). Therefore, the present findings reconfirm the findings by Schrauzer et al. (1994).

It should be emphasized that the significant decrease in serum creatinine levels indicates the dilution of the subjects' serum by drinking mineral water. That is, the change in the mean creatinine level from 0.689 to 0.640 mg/dL means 108 % of dilution. If this is the case in serum BDNF levels, then the mean BDNF might have been changed from 22.7 to 21.1 ng/mL. However, BDNF was apparently unchanged from 22.7 to 22.5 ng/mL. This suggests that there was a substantial increase of BDNF which might have compensated for the difference between 22.5 and 21.1 (i.e. 1.4 ng/mL).

Although BDNF is highly concentrated in the nervous system, it is also found in the serum of humans and other mammals, where its function is poorly understood (Karege et al., 2005). Pan et al. (1998) reported that BDNF can cross the blood-brain barrier and Karege et al. (2002) reported a positive correlation between serum and cortical BDNF levels in animal studies. Recently, Karege et al. (2005) also reported a decrease in serum BDNF levels without a change in the whole blood BDNF content of drug-free depressed patients, indicating the involvement of BDNF release from platelets. In the present study, it seems likely that the above substantial increase (although seemingly unchanged) in serum BDNF levels was induced by BDNF release from the subjects' platelets. It is also possible that in their brain BDNF release was concurrently increased and improved their mental state after lithium absorption during drinking lithium mineral water.

There are several limitations to the present study. First, the psychological findings may have been influenced by the nature of an open study. We, however, explained both effects and side effects of lithium to the subjects openly and, to begin with, they came to the springs and drank mineral water in order to maintain their physical health but not mental health. Therefore, it seems unlikely that their psychological reactions influenced subjective ratings although placebo effects cannot be denied completely. Second, the study population was not selected randomly and the design did not have control (e.g. drinking tap water). Third, the time of drinking (2–3 to 6–7 AM) overlapped with that of partial sleep deprivation. Although it cannot be denied completely, the significant association between serum lithium and BDNF levels supports the involvement of drinking lithium mineral water. Finally, our subjects were healthy volunteers and Schrauzer et al.'s (1994) subjects had a history of substance dependence, which were different from bipolar disorders. This difference might have affected the difference of therapeutic lithium levels.

The present findings suggest that drinking mineral water containing very low lithium levels may increase serum lithium levels and improve mental state as a likely consequence of changes in BDNF levels. Taking several methodological limitations into consideration, further studies are required to confirm this suggestion.

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