

# Lactose Malabsorption Is Associated with Early Signs of Mental Depression in Females

## A Preliminary Report

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Lactose malabsorption is characterized by a deficiency of mucosal lactase. As a consequence, lactose reaches the colon where it is broken down by bacteria to short-chain fatty acids, CO<sub>2</sub>, and H<sub>2</sub>. Bloating, cramps, osmotic diarrhea, and other symptoms of irritable bowel syndrome are the consequence and can be seen in about 50% of lactose malabsorbers. Having made the observation that females with lactose malabsorption not only showed signs of irritable bowel syndrome but also signs of premenstrual syndrome and mental depression, it was of interest to establish whether a statistical correlation existed between lactose malabsorption and mental depression. Thirty female volunteers were analyzed by measuring breath H<sub>2</sub> concentrations after an oral dose of 50 g lactose and were classified as normals or lactose malabsorbers according to their breath H<sub>2</sub> concentrations. All patients filled out a Beck's depression inventory questionnaire. Of the 30 female volunteers, six were lactose intolerant (20%) and 24 were normal lactose absorbers (80%). Subjects with lactose malabsorption showed a significantly higher score in the Beck's depression inventory than normal lactose absorbers did. The data thus suggest that lactose malabsorption may play a role in the development of mental depression. In lactose malabsorption high intestinal lactose concentrations may interfere with L-tryptophan metabolism and 5-hydroxytryptamine (serotonin) availability. Lactose malabsorption should be considered in patients with signs of mental depression.

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**KEY WORDS:** depression; lactose malabsorption; lactose load.

Lactose malabsorption syndrome is a well-described gastrointestinal disorder that can be seen either as a primary deficiency of lactase (genetic or familial) or as a secondary (acquired) deficiency of lactase due to other gastrointestinal disorders (1). Patients with lactose malabsorption are not able to cleave and conse-

quently absorb the ingested disaccharide adequately, so large quantities of lactose reach the colon, where it is broken down by colon bacteria into short-chain fatty acids, CO<sub>2</sub> and H<sub>2</sub>, which can be measured in the expired air. Bloating, abdominal discomfort, and sometimes osmotic diarrhea are the consequences induced by the degradation products produced by the colonic bacteria.

The diagnosis of lactose malabsorption can easily be made by measuring the H<sub>2</sub> concentration in exhaled breath after an oral load of lactose (2). Having made the observation that female patients who suffered from lactose malabsorption also often showed

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clinical signs of mental depression, it was of interest to establish whether a statistical correlation existed between the two clinical entities.

## MATERIALS AND METHODS

**Patients.** Thirty otherwise healthy female outpatients who visited the physician's office for a medical health check-up were studied. The patients were aged from 16 to 60 years (mean 43.6 years). None of the patients showed signs of inflammatory bowel disease or any other chronic disease or infectious diseases and were therefore classified as primary lactase deficient. No patients were under medication. All patients filled out a Beck's depression inventory questionnaire (3).

**H<sub>2</sub> Breath Tests.** All tests were done between 8:00 and 8:30 AM, and body weight and height were measured at the beginning of the trials. After a 12-hr overnight fast the H<sub>2</sub> breath test was performed with an oral dose of 50 g lactose given in 250 ml of tap water. Breath H<sub>2</sub> was measured using a Bedfont gastrolizer (Bedfont Ltd., Kent, ME9 7HN, UK) before lactose load and at 30-min intervals for at least 2 hr after lactose load. Maximum breath H<sub>2</sub> concentrations were registered (H<sub>2</sub>-max) and the differences from baseline values were calculated ( $\Delta$ -H<sub>2</sub>). The H<sub>2</sub> monitor used has been validated by several authors (4–6).

**Data Analysis.** Breath H<sub>2</sub> concentrations greater than 20 ppm over baseline after lactose load was used as a cut off for the diagnosis of lactose malabsorption (7). Subjects with a rise of breath H<sub>2</sub> concentrations  $\leq$ 20 ppm over baseline were considered to be normal lactose absorbers. The *t* test for independent samples was calculated and linear regression analysis was performed using a standard PC statistical program (STATISTICA for windows version 5.0) (8). In addition, nonparametric tests (Mann-Whitney U test and Spearman rank correlation analysis) were performed for conformation (data not shown), and the results agreed well with each other.

## RESULTS

Six patients had breath H<sub>2</sub> concentrations  $>$ 20 ppm over basal fasting values and were classified as lactase deficient (Table 1). The remaining 24 subjects had maximum breath H<sub>2</sub> concentrations  $\leq$ 20 ppm over their baseline value and were therefore classified as normal lactose absorbers.

Mean body mass index (BMI) was 25.24 ( $\pm$  3.8 SEM) for lactose-intolerant subjects and 22.8 ( $\pm$  0.7 SEM) for normals. There was a slight but significant correlation ( $r = 0.41$ ,  $P < 0.05$ ) between BMI and lactose absorption with a trend for a higher BMI of lactose-intolerant individuals.

The Beck's inventory depression score was significantly higher ( $P < 0.001$ ) in lactose-intolerant subjects, with a mean score of 21.2 ( $\pm$ 11.3 SD) than in normals with a mean score of 9.25 ( $\pm$ 5.4 SD) (Figure

TABLE 1. PATIENT CHARACTERISTICS, DEPRESSION SCORE, AND BREATH H<sub>2</sub> CONCENTRATIONS AFTER LACTOSE LOAD

	N	Mean	Minimum	Maximum	SD
Lactose malabsorbers					
Age	6	45.00	35.00	57.00	7.67
Body mass index	6	25.24	19.81	43.87	9.33
Depression score	6	21.17	10.00	38.00	11.32
$\Delta$ H <sub>2</sub>	6	71.50	24.00	113.00	37.61
H <sub>2</sub> -max	6	72.67	24.00	113.00	37.61
Normals					
Age	24	43.29	16.00	60.00	11.13
Body mass index	24	22.82	17.63	29.73	3.43
Depression score	24	9.25	0.00	24.00	5.38
$\Delta$ H <sub>2</sub>	24	0.875	-8.00	6.00	2.68
H <sub>2</sub> -max	24	3.96	0.00	24.00	5.52

1). Linear regression analysis between Beck's depression score and the maximum breath H<sub>2</sub> concentrations showed a fairly high and significant correlation ( $r = 0.73$ ,  $P < 0.05$ ) (Figure 2). Change over baseline breath H<sub>2</sub> concentrations also correlated with Beck's depression score ( $r = 0.67$ ,  $P < 0.05$ ), but the correlation coefficient was not as high as with the maximum breath H<sub>2</sub> concentrations.

## DISCUSSION

The data in the present study show that lactose malabsorption is significantly associated with a score for mental depression. Since depression may be related with impaired 5-hydroxytryptamine (serotonin) metabolism (9), the data suggest that the lactose malabsorption interferes with the L-tryptophan availability. It has been shown in several studies, that L-tryptophan depletion may induce depression (10–12) and premenstrual syndrome (13).

The so-called Maillard reaction may provide an explanation for the association between lactose malabsorption and disturbed tryptophan metabolism: Lactose, like other reducing sugars, reacts with proteins and amino acids such as L-tryptophan (14), resulting in a decrease in protein quality due to the loss of amino acid residues and decreased protein digestibility. Maillard products can also inhibit the uptake and metabolism of free amino acids such as L-tryptophan and of other nutrients such as zinc (15). The formation of a lactose-L-tryptophan complex has been previously described (16). As lactose malabsorbers have high intestinal lactose concentrations and lactose can easily bind to L-tryptophan, the probab-

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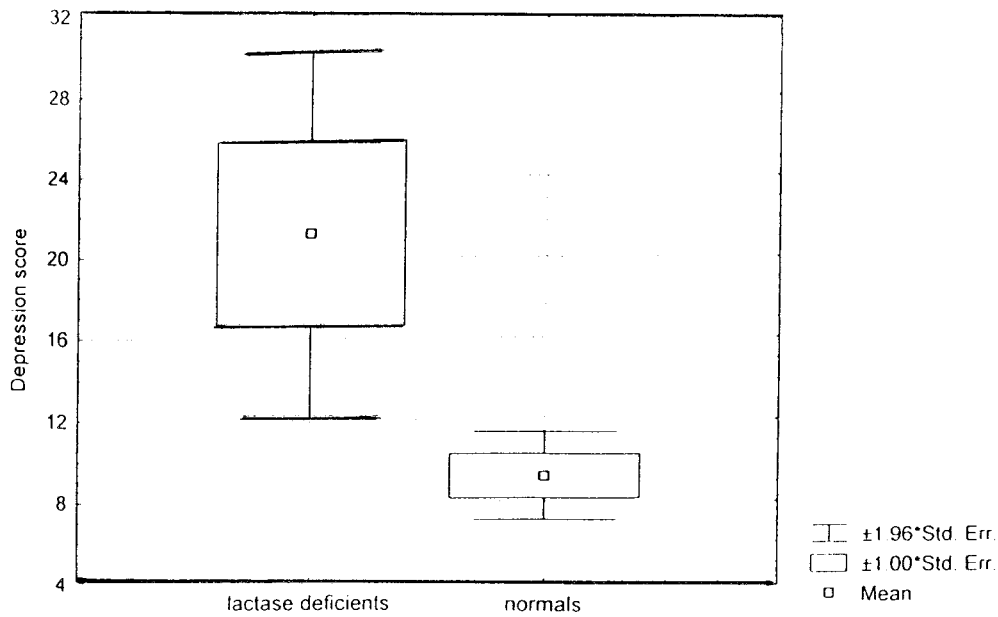


Fig 1. Different depression scores in lactase-deficient and normal females.

ity for forming the nonabsorbable lactose-L-tryptophan complex rises. As a consequence, not only lactose but also L-tryptophan is absorbed to a lesser extent.

Interestingly the association of lactose malabsorption with mental depression is only significant in females ( $P < 0.001$ ). We did not find such a relationship in men (data not shown). This is in line with findings of sex differences in mood responses to acute

tryptophan depletion by several authors (11, 13, 17) and may serve as a further argument that lactose malabsorption interferes with L-tryptophan metabolism. In females normal concentrations of serum L-tryptophan were found to be lower than in males (18). This is probably due to a higher activity of the hepatic tryptophan-2,3-dioxygenase (= tryptophan pyrrolase), which is estrogen dependent. Estrogens have a stimulatory effect on this enzyme, thus shifting the

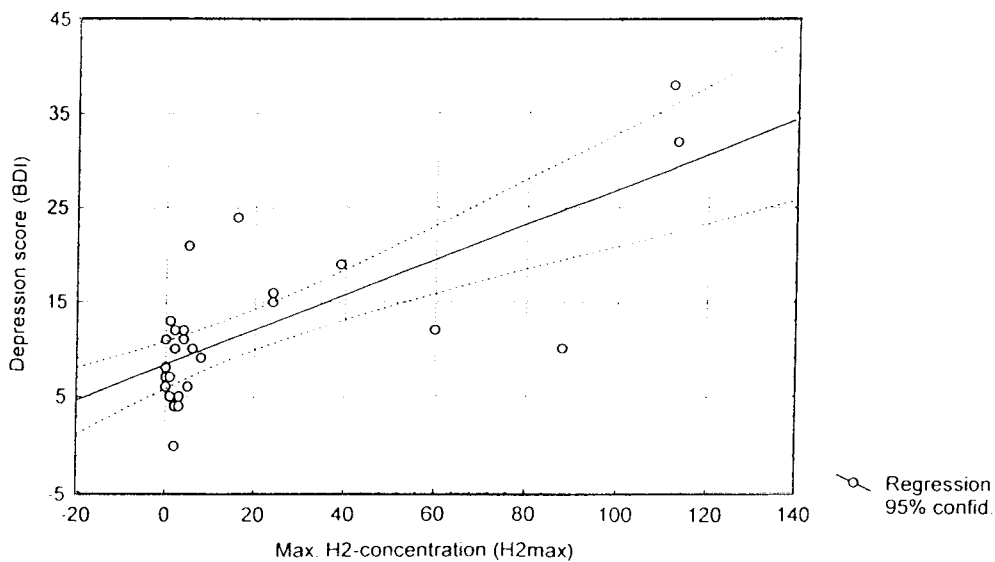


Fig 2. Depression score vs max  $H_2$  concentration.  $BDI = 8.3404 + 0.18604 \cdot H_2max$ . Correlation:  $r = 0.72772$ ;  $P < 0.05$ .

L-tryptophan metabolism away from the 5-hydroxytryptophan synthesis [precursor of 5-hydroxytryptamine (serotonin)] and towards the kynurenine pathway.

A deficiency of 5-hydroxytryptamine (serotonin) would also provide an explanation for the association found between higher BMI and lactose malabsorption. Hunger for carbohydrates, sweets, chocolate, and sweet milk products is a well-known symptom of patients with mental depression. Individuals who experience dysphoric mood as a function of low levels of brain 5-hydroxytryptamine may seek out carbohydrate-rich foods to alter their mood state (19). Carbohydrate consumption increases the availability of the amino acid L-tryptophan, which in turn increases brain 5-hydroxytryptamine levels (19). As modern food processing involves replacement of regular sugar in sweet foods with lactose, the hunger for (sweet) carbohydrates may lead to a vicious circle of worsened lactose malabsorption and consequent L-tryptophan depletion. Measurements of tryptophan and serotonin concentrations will be necessary to explore and confirm a role for these compounds in the association between lactose malabsorption and depression.

Another explanation for the development of depressive signs could be the formation of toxic bacterial degradation products that may be formed when amino acids-carbohydrate compounds reach the colon, possibly interfering with neurotransmitter metabolism. The development of mental depression could also be enhanced by micronutrient deficiencies as lactose malabsorption, as well as fructose malabsorption, is often associated with decreased oro-cecal transit time, thus decreasing the mucosal contact time of micronutrients. This could lead to vitamin or oligo-element deficiencies. Interestingly, an increased frequency of signs of depression was also found in subjects with fructose malabsorption (20).

Lactose malabsorption is very frequent in the general population. Its prevalence varies in different ethnic groups and is found in northern Europe with a prevalence of 3-5%, in central Europe with prevalence of 5-15%, and in the population of Mediterranean countries sometimes with a prevalence of more than 70%. In Africa and Asia lactose malabsorption is found in up to 40-100% of the population. According to our findings this could lead to the suggestion that all these people should all have a higher risk for developing mental depression.

The present study shows a significant correlation between lactose malabsorption and the score for

mental depression. Correlations do not necessarily reflect a cause-effect relationship, and both conditions may result from another yet unknown cause. However, The data suggest lactose may possibly interfere with L-tryptophan metabolism and hence 5-hydroxytryptamine synthesis. Lactose malabsorption should be considered in patients with mental depression or premenstrual syndrome.

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