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# The Thyroid, Magnesium and Calcium in Major Depression

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## Introduction

Thyroid hormones have been implicated in the biology of depressive illness (Joffe and Levitt 1993). Although the pathophysiological significance of these changes remains uncertain, most studies agree that circulating thyroxine (T4) and free T4 levels are increased in depressed patients and decrease with recovery (Bauer and Whybrow 1987; Joffe and Levitt 1993).

Both magnesium ( $Mg^{++}$ ) and calcium ( $Ca^{++}$ ) are cations which occur abundantly in the body and are implicated in numerous cellular functions including the regulation of various neurotransmitters. Several studies have examined serum  $Mg^{++}$  and 78 serum  $Ca^{++}$  in depression. With regard to calcium there is a reasonable consensus among studies that serum  $Ca^{++}$  levels are increased in depression and decrease with recovery (Carman et al 1977; Faragalla and Flach 1977; Linder et al 1989). Data on serum  $Mg^{++}$  levels have been more inconsistent and both increases and decreases have been observed in depressed patients (Frazer et al 1983; Frizel et al 1969; Widmer et al 1994).

There is evidence that the thyroid axis may influence both magnesium and calcium metabolism (Mosekilde and Christensen 1977; Wiang et al 1992). Furthermore, in a preliminary report, Hasey et al (1993) reported an inverse correlation between T4 and serum  $Mg^{++}$  levels in 13 depressed patients. We therefore decided to extend these preliminary findings (Hasey et al 1993) and evaluate the relationship between serum levels of these two cations and circulating thyroid hormones in a large cohort of well-described and unmedicated patients with unipolar major depressive disorder.

## Methods

### Subjects

One hundred thirty-five consecutive outpatients, 41 men and 94 women, aged  $39.1 \pm 10$  years (mean  $\pm$  SD), consented to participate in this study while attending the Mood Disorders Program at the University of Toronto. All subjects fulfilled Research Diagnostic Criteria for unipolar non-psychotic major depressive disorder, unipolar subtype as determined by a structured interview using the Schedule for Affective Disorders and Schizophrenia-Lifetime Version (SADS-L). At the time of assessment, all subjects included had a minimum score of 16 on the 17-item Hamilton Rating Scale for Depression (HAMD). All subjects were medication free a minimum of 2 weeks and had not received lithium for at least 6 weeks. Patients were excluded from the study if they had a recent, within 3-month history of substance abuse or any medical disorder which would affect the measurement of serum cations or thyroid hormone levels. No subjects were receiving calcium or other mineral supplements.

### Procedure

At the time of completion of the diagnostic interview and the HAMD, blood was drawn from measurement of serum  $Mg^{++}$  and  $Ca^{++}$  levels as well as thyroid hormone levels by assays previously described (Joffe and Singer 1990). As the data were not normally distributed, Spearman correlational analyses were used to examine the relationship between  $Mg^{++}$ ,  $Ca^{++}$ , and thyroid hormone levels.

## Results

There was a significant positive correlation between serum  $Mg^{++}$  and T4 levels ( $r = 0.20$ ,  $df = 134$ ,  $p < 0.05$ ) (see Figure 1). There was no significant correlation between serum  $Ca^{++}$  and circulating thyroid hormone levels either T4, triiodothyro-

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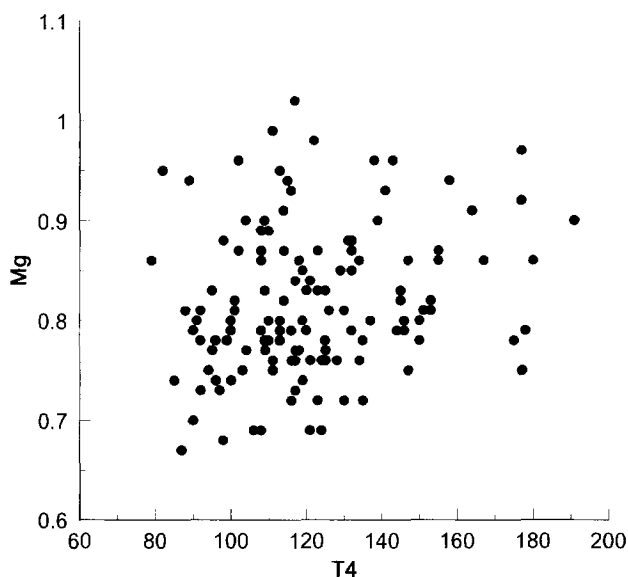


Figure 1. Significant correlation between serum magnesium and thyroxine in 135 subjects with major depression. Spearman rank order correlation  $r = 0.20$ ,  $p < 0.05$ .

nine (T3), or thyrotropin (TSH). Furthermore, neither the serum  $Mg^{++}$  nor the serum  $Ca^{++}$  levels correlated with either age or severity of depression as measured by the HAMD.

When the correlation between serum magnesium and T4 was examined by gender, it was significant for women ( $r = 0.28$ ,  $df = 93$ ,  $p < 0.01$ ) but not for men ( $r = 0.14$ ,  $df = 40$ ,  $p > 0.05$ ).

For the total sample, the mean serum magnesium level was  $0.82 \pm 0.07$  mmol/L and the mean serum calcium was  $2.41 \pm 0.08$  mmol/L. The mean values for thyroid hormone measurements were: T4,  $121.6 \pm 24.9$  mmol/L, T3,  $2.4 \pm 0.4$  mmol/L

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and TSH,  $1.92 \pm 1.24$  uU/mL. The mean HAMD score for the group was  $19.7 \pm 3.8$  (range 16-32).

## Discussion

In a large sample of unmedicated patients with mild to moderate primary major depressive disorder we observed a significant correlation between mean serum  $Mg^{++}$  levels and mean circulating T4 levels. There was no significant correlation between any of the other thyroid indices and either serum  $Mg^{++}$  or  $Ca^{++}$ . The thyroid axis is known to regulate magnesium metabolism (Wiang et al 1992) possibly by regulation of the transport of magnesium from extracellular to intracellular fluid compartments (Hasey et al 1993). Our observations are consistent with these data and extend this relationship to depressed patients notwithstanding the fact that abnormalities of both thyroid hormone levels (Bauer and Whybrow 1987; Joffe and Levitt 1993) and magnesium levels (Frazer et al 1983; Frizel et al 1969; Widmer et al 1994) have been reported in this diagnostic group. Our findings contrast with Hasey et al (1993) who reported an inverse correlation between serum magnesium and T4 in 13 subjects with affective disorders. The difference between our findings are unclear but may be due to several factors including our much larger sample size and differences in the clinical characteristics of our samples.

For T4, and to a lesser extent serum  $Mg^{++}$ , the most consistent changes have been observed with response to antidepressant treatment. To clarify the role of thyroid hormones and magnesium and their interrelationship in the biological basis of depressive illness and the response to antidepressant treatment, future studies should examine the relationship between potential changes in serum magnesium and circulating thyroid hormone levels with antidepressant treatment and particularly in relationship to treatment response.